ERECTILE DYSFUNCTION

diagnosis and treatment

MF van Driel

ERECTILE DYSFUNCTION

STELLINGEN

behorende bij het proefschrift van Mels Frank van Driel

ERECTILE DYSFUNCTION

1 L'impuissance, c'est mourir un petit peu.

2 Het roken van sigaretten kan de erectie zeer nadelig beïnvloeden.
Dr.K.P. Juenemann et al., Journal of Urology 1987; 138: 438–41

3 Priapus was in de Griekse oudheid onder meer de god van de bijenteelt. Het is op zijn minst bijzonder dat thans het fenomeen van Priapus met een prik kan worden bestreden.

4 Vaatchirurgen nemen nogal eens de benen voor seks.

5 Als de arts in de urethra de rechte weg verlaat, heeft de patiënt smart op smart te vrezen.

6 Het artsenberoep vergt van zijn beoefenaars toewijding, meer dan de doorsnee beroepen dat doen. Wie dat niet wil moet geen arts worden.
Prof.Dr.H.M.Kuitert in zijn boek "Mag alles wat kan?" (1989)

7 Bij het selecteren van aanstaand urologen zou het besef dat er in de urologie steeds minder bloed gaat vloeien een belangrijke rol moeten spelen.

8 Bij de vrouw is het optreden van dysurie en pollakisurie na de coïtus verdacht voor het bestaan van een urethradivertikel.

9 De aangeboren afwezigheid of hypoplasie van de musculus depressor anguli oris wordt ten onrechte nog al eens voor een partiële verlamming van de nervus facialis aangezien.

10 Het resultaat van hyposensibilisatie voor wespegif kan slechts goed beoordeeld worden na een echte steek.

11 Perfectioneren van de reeds bij apen geteste erectiepacemaker zal uiteindelijk de "chipwip" mogelijk maken.
naar Peter Hofstede, Haagse Post, 5 november 1988.

12 Ondanks zijn harde uiterlijk is de schildpad een tedere minnaar.

RIJKSUNIVERSITEIT GRONINGEN

ERECTILE DYSFUNCTION

Diagnosis and Treatment

PROEFSCHRIFT

ter verkrijging van het doctoraat in de Geneeskunde
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To
Frank
Tom and
Koen

CONTENTS

PREFACE

Knowledge of sick and healthy bodies is the basis of medical science. Knowledge of the human body and its epistemology are of a scientific nature. This gives medical science a technical character: to handle methodically a biologically defined organism in a diagnostic situation and to administer medicines or subject it to surgery, by way of scientific experiment. The treatment of sick people in this way is obviously unsatisfactory. This is why for some decades medical science has been trying to dissociate itself from such an overly medico-technical approach of sick people. The Cartesian doctrine of the dualism of body and soul — the body as a material object offered to science for the purposes of research and, if necessary, mending — had to be abandoned. Instead it was held in favour of 'the whole of man' as the object of medical care. The advantage of this approach is evident: the sick person is at least treated as a person and as a human being. However, when the urologist is dealing with a sick man, he is not, nor should he be responsible for the entire man. For reasons of competence and division of labour a touch of Cartesianism is inevitable and indispensable. For instance if the urologist tries to concern himself with the entire man in a case of erectile dysfunction, both doctor and patient will come to grief, and it is not what the urologist was trained for.

Interpersonal relations will be involved in many symptoms of erectile dysfunction. Urologists should realise this when they try to formulate a proper diagnosis and therapy. They should be able to understand erectile dysfunction-related complaints. But being able to understand does not imply the ability to cure. The urologists should confine to his subsection, not the entire man. If necessary they should involve sexologists, psychologists and psychiatrists, and above all the patient's partner!

A urologist pursuing treatment of more than a subsection of functional disorders and urogenital functions will turn his profession into an all-embracing art and himself into a 'priest' mediating between fate and salvation. Not as in former times, with the aid of magic, but with the application of medical and surgical techniques.

The problem of the doctor's so-called undivided loyalty to his patient is assuming new proportions these days due to the ever-increasing expansion of medical knowledge and capacity. For instance, financial shortages limit the number of patients with erectile dysfunction to be treated surgically with a modern, inflatable, erection prosthesis. This appears to be a subject of tacit agreement in the Netherlands. Decisions are made on the individual patient. It seems that only the affluent can afford to have a modern erection prosthesis implanted. With an eye to justice the following rule of thumb should be applied: as long as there is no opportunity for all patients to benefit equally from new knowledge and capacities, introduction thereof should be delayed until an equal opportunity is provided. It is a kind of practical (negative) test: when a given treatment is not available on the national medical insurance scheme, it certainly fails the requirements of just distribution of scanty finances.

Medical actions are small-scale actions. They should, as Kuitert in his medico-ethical considerations formulates, provide help to escape from 'the evil'.[1] This presupposes a urologist conscious of the limitations of his profession, he is not omnipotent and should not be seen so. There will always be patients with disorders including erectile dysfunction, who are incurable. Why, is the urologist's duty to explain to this patients. Also if he fails to point out the limitations of his care to his patient both will suffer for it. For example, intracavernous papaverine injections will not improve or heighten the feeling of orgasm. This point should be made explicit.

There is still another way to manage the limits of medical action: patients can help themselves to escape the 'evil' of a physical ailment. It presupposes some self-help, some enterprise on the patient's part and, with respect to erectile dysfunction, some insight into the immutable conditions of natural processes like ageing.

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CHAPTER 1

INTRODUCTION

Over the last decade, there have been appreciable advances in the understanding of the physiology of penile erection. It is now realized that penile erection is a complex physiologic response depending upon the integration of vascular, neurologic and endocrine mechanisms, and influenced by the psychological state. Although many aspects of the neurohumoral control of erection are still unknown, it is clear that penile erection can be triggered by a variety of psychogenic and reflexogenic stimuli. They cause a neurally mediated dilatation of the penile blood vessels leading to an increase in blood flow, relaxation of the smooth muscle cells in the corpora cavernosa and reduction of venous drainage by the specific anatomy of the venous system of the corpora cavernosa.

Adequate erectile functioning means the ability to initiate, sustain and successfully conclude the coital act. This implies, a satisfactorily rigid penile erection sufficiently sustained to secure intromission with subsequent orgasm. A weak and/or unsustained erection, a deformed erection, as in Peyronie's disease and congenital curvature, and priapism, constitute different types of erectile dysfunction. Peyronie's disease is an ideopathic dense fibrosis of the areolar connective tissue between or within the tunica albuginea and the corpus cavernosum. Priapism, a rather uncommon form of erectile dysfunction, is a persistent erection, accompanied by pain and tenderness, which fails to subside even after climax.

Very little is known about the number of men having problems with erection. Probably it concerns occasionally almost every man in his life. This may be just once or during a short period and can be caused by psychological problems or a disease. Fortunately such an erection problem often passes away without any specific aid or treatment. A primary erection problem from early on in adolescence is rare. It is estimated to occur in about one out of 700 men.[1] Secundary erection problems, originating later in life certainly occur more frequently. In an American investigation of 100 men (mean age of 36 years) seven percent stated to have difficulties in getting an erection and nine percent in maintaining it.[2] How often they had these problems and how seriously they considered them is not clear. In the Netherlands Frenken e.a. examined 250 men at the age of 18–55 years (mean age 36).[3] Sixteen percent had occasionally troubles to get excited or to stay excited during intercourse. The percentage of men who failed to get excited or to get an erection at all was 6%. We may assume that among the young and middle-aged men almost six percent have erection problems regularly to permanently, while another 10–16% are troubled with it occasionally.[2,3,4,5]

A man does not retain his full youthful erectile capacities all his life. There are certain inevitable age-related changes: the erection becomes softer; the threshold for stimulation increases; the lenght of time that the erection can be maintained decreases; and the erectile mechanism becomes more vulnerable to emotional stress.[6] So, we do know that the possibility of erection problems increases with age.

The frequency of intercourse is not a true measure for adequate erectile functioning, since it depends on many extraneous factors and involves mutual agreement. In many males frequency of intercourse is related to age and usually decreases as the years progress. Actually, the height of erectile potency is in the age of the early twenties and tapers off slowly from that time on.[5] Frequency of intercourse may also be dependent on relaxation and freedom from the strains and tensions of modern western society, although already Hippocrates stated in his time that impotence could be caused by preoccupation with business.[7]

Until the 1970s, when combined efforts of urology and industrial technology produced several types of silicone based intracavernous erection prostheses,[8,9,10] the interest of urologists in patients with erectile dysfunction was limited. The serendipitous discovery that papaverine injected into the corpora cavernosa produced erection ushered in the era of intracavernous injection therapy in the early 1980s.[9] Especially this therapeutic option promoted laboratory research, increased clinical activity, and formation of multidisciplinary teams, including endocrinologists, vascular surgeons, urologists, psychiatrists, psychologists and sexologists. It caused significant progress in diagnosis and treatment of the varieties of erectile dysfunction. However, many questions remain to be answered, especially concerning the long term results of prosthetic surgery, arterial reconstruction and intracavernous self-injection therapy.

This thesis attempts to provide a comprehensive overview of the recent advances in diagnosis and treatment of erectile dysfunction. Clinical studies about 3 types of erectile dysfunction — erectile impotence, a bent penis in erection and priapism — as well as the therapeutic outcome were performed.

The following issues were investigated:

- The physiology of normal erection (chapter 2)
- The diagnosis and treatment of erectile dysfunction (chapter 3)
- Mythologic, religious, and cultural aspects of impotence before the present modern era (chapter 4)
- The value of simple penile blood pressure measuring with regard to the outcome of intracavernous papaverine injection (chapter 5)
- The complications of intracavernous self-injection therapy, the impact of this therapy upon sexual and psychological functioning and the reasons for discontinuation (chapter 6).
- The results of intracavernous self-injection of papaverine in the treatment of erectile impotence after major pelvic surgery (chapter 7).
- The treatment of erectile dysfunction in patients with Peyronie's disease and congenital penile curvature (chapter 8).
- The treatment of priapism by injection of adrenaline into the corpora cavernosa (chapter 9).

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CHAPTER 2

THE PHYSIOLOGY OF PENILE ERECTION

A. INTRODUCTION

The physiology of penile erection involves a complex interaction of the vascular, neurologic and hormonal systems. Over the last decade there have been appreciable advances in the understanding of penile erection. It is now realized that the tone of the smooth muscle in the sinusoidal system of the corpora cavernosa plays a major role in the control of the flaccid and erect states. Although many aspects of the neurohumoral control of erection are still unknown, it is clear that an erection can be triggered by a variety of psychogenic and reflexogenic stimuli. They produce a neurally mediated dilatation of the penile arteries and arterioles and a neurally mediated relaxation of the smooth muscles of the sinusoidal system of the corpora cavernosa leading to an increase in flow and distension of the penis. In this chapter anatomy and current knowledge about the physiology of erection will be summarized.

B. ANATOMY

B_1 Arterial supply

The blood supply to the penis is entirely from the internal pudendal artery except for some minor scrotal and epigastric arterial branches.[1] In most men this artery arises from the lowest division of the ischiopudendal trunk of the internal iliacal artery at the level of the sacroiliac joint. This internal pudendal artery can be divided into four segments: the pelvic, gluteal, ischiorectal and perineal. The pelvic segment is directed towards the ischial spine. The gluteal segment begins at the lower part of the greater sciatic foramen and crosses the back of the tip of the ischial spine and enters the perineum through the lesser sciatic foramen. The ischiorectal segment passes through the pudendal (Alcock's) canal in the ischiorectal fossa and is hence named the perineal segment. At the level of the urogenital diaphragm the perineal segment of the internal pudendal artery divides into four terminal branches: the dorsal artery, the urethral (spongiosal) artery, the deep (cavernous) artery, and the bulbar artery (figure 1).

The dorsal artery enters the penis and continues distally beneath Buck's fascia, between the centrally located deep dorsal vein and the paired dorsal nerves. It is responsible for engorgement of the glans penis during erection. The spongiosal or urethral artery runs longitudinally through the corpus spongiosum lateral to the urethra. Along its course it supplies the corpus spongiosum, the urethral tissues and the glans penis.

The cavernous or deep artery of the penis penetrates the tunica albuginea in the crurae. It supplies blood to the erectile tissue of the corpora cavernosa. On entering the corpora cavernosa the cavernous artery divides into multiple tortu-

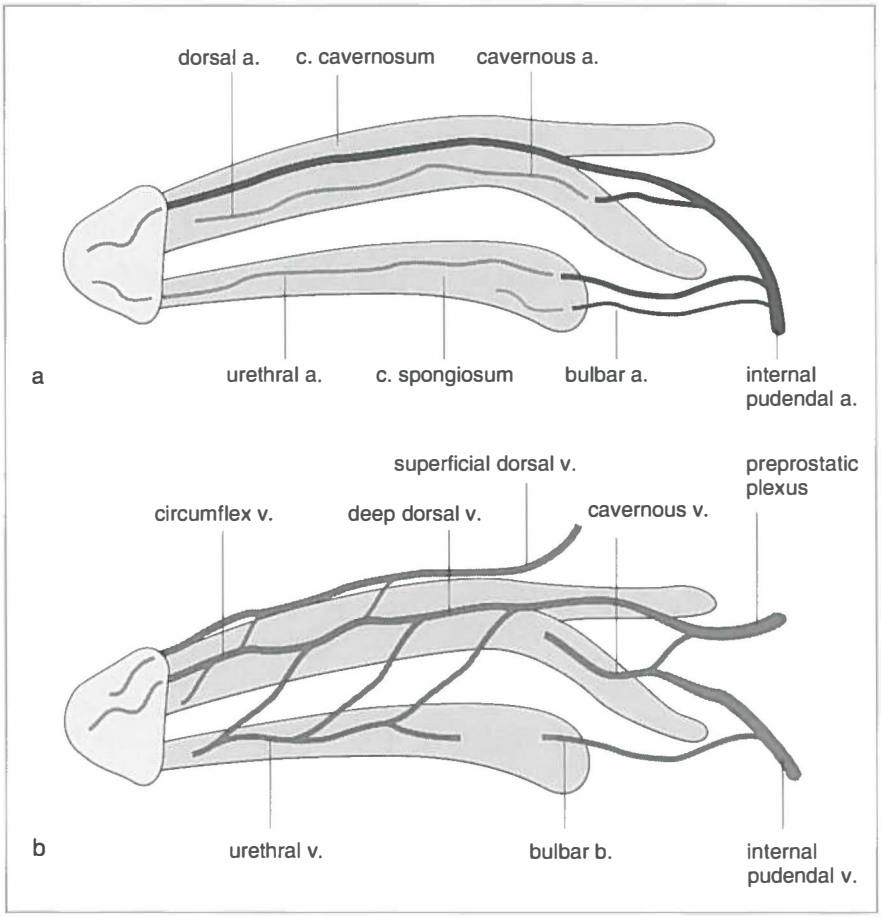

Figure 1 **a.** Arterial supply
b. Venous return

ous terminal branches known as the helicine arteries (so named because of their spiral appearance in the flaccid penis). These terminal arterioles empty into the sinusoidal spaces of the corpora cavernosa (figure 2).

The bulbar artery enters the bulb of the penis shortly after its origin. It supplies blood to Cowper's gland and the proximal urethral bulb.

B_2 Venous drainage

Venous outflow from the penis proceeds through three main sets of veins: the superficial, intermediate, and deep veins, each with multiple interconnections (figure 1). The superficial dorsal vein drains the skin and subcutaneous tissues superficial

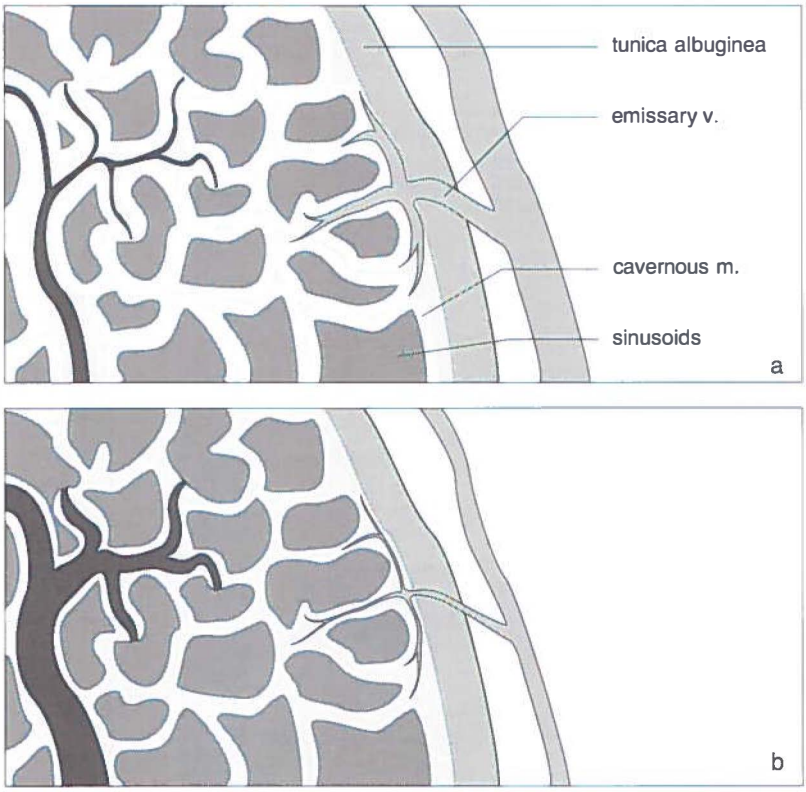

Figure 2 **a.** In the flaccid state the arteries, arterioles are contracted. The intersinusoidal and subtunical venular plexuses are open with free flow to the emissary veins.
b. In the erect state the muscles of the sinusoidal wall and the arterioles relax, allowing maximal flow to fill the now-compliant sinusoidal spaces. The small veins are compressed between the sinusoids. The larger intermediary veins are sandwiched and compressed between the distended sinusoidal wall and the non-compliant tunica albuginea thus restricts the venous flow to a minimum.

to Buck's fascia. It drains into the superficial external pudendal vein, a branch of the saphenous vein. The intermediate set of veins run under Buck's fascia but superficial to the tunica albuginea which envelops the corpora cavernosa. Approximately 6 to 15 veins emerge from the glans penis and form a subcoronal plexus which drains into the main intermediate channel, the deep dorsal vein. Also draining into the deep dorsal vein is a series of emissary and circumflex veins from the corpora cavernosa. The deep dorsal vein courses proximally in the midline between the two corpora to empty into the periprostatic plexus of Santorini. The deep venous system drains both the corpora cavernosa and the corpus spongiosum. The sinusoidal spaces are drained through a set of emissary veins which traverse to the tunica albuginea (figure 2). They vary in diameter: the thinner veins are lined with

endothelium only while the larger ones also have a thin longitudinal smooth muscle wall. Some of these emissary veins follow a straight path, whereas others run obliquely through the tunica albuginea. In the mid- and distal part of the penis they join to form the circumflex veins, which empty into the deep dorsal vein. Some of the emissary veins drain into the deep dorsal vein directly. In the proximal part of the penis the emissary veins form the cavernous vein, which empties into the internal pudendal vein. The corpus spongiosum drains through a set of deep bulbar and urethral veins.

B_3 The sinusoidal system

The sinusoids are irregularly shaped spaces surrounded by trabeculae that consist of bundles of smooth muscle, elastic fibers, collagen, and loose areolar tissue containing numerous arterioles and nerves. The sinusoids contain blood and are lined by flat cells similar to the endothelial lining of veins. They are considered intrinsically active contractile units, sensitive to neural stimuli, and accordingly they play an important role in erection and detumescence.[1]

B_4 Fascial covering

Each corpus cavernosum is encapsulated by its own tunica albuginea, which consists of thick collagenous fibers. The increase in blood volume within the corpora cavernosa during an erection is limited by the length and circumference to which the tunica albuginea can be stretched. During the rigid phase the tunica compresses the emissary veins thereby reducing the drainage of the intracavernous blood (figure 2).

The tunica albuginea of the corpus spongiosum is much thinner than that of the cavernosa. The glans penis has practically no tunica albuginea and only a minimal amount of fibrous tissue between the sinusoids and the epidermis.

B_5 Nerve supply

The autonomic innervation of the penis arises from the pelvic plexus, which is formed by parasympathic visceral efferent preganglionic fibers that arise from the sacral centre (S2 to S4) and sympathetic fibers from the thoracolumbar centre (Th 11 to L2)(figure 3).

The combined parasympathetic nerves enter the plexus via the pelvic nerve. The sympathetic contribution to the pelvic plexus comes from the thoracolumbar centre and reaches the pelvic plexus by 3 pathways: 1. the hypogastric nerve (which is the most important), 2. branches from the sacral sympathetic chain (most commonly from the fourth and fifth ganglia and 3. branches that accompany the superior hemorrhoidal artery (which originate from the autonomic inferior mesenteric plexus).

The pelvic plexus is a 4 to 5 cm curvilinear or rectangular network lying in the pelvic fascia on either side of the lower genitourinary tract and rectum. Connective tissue

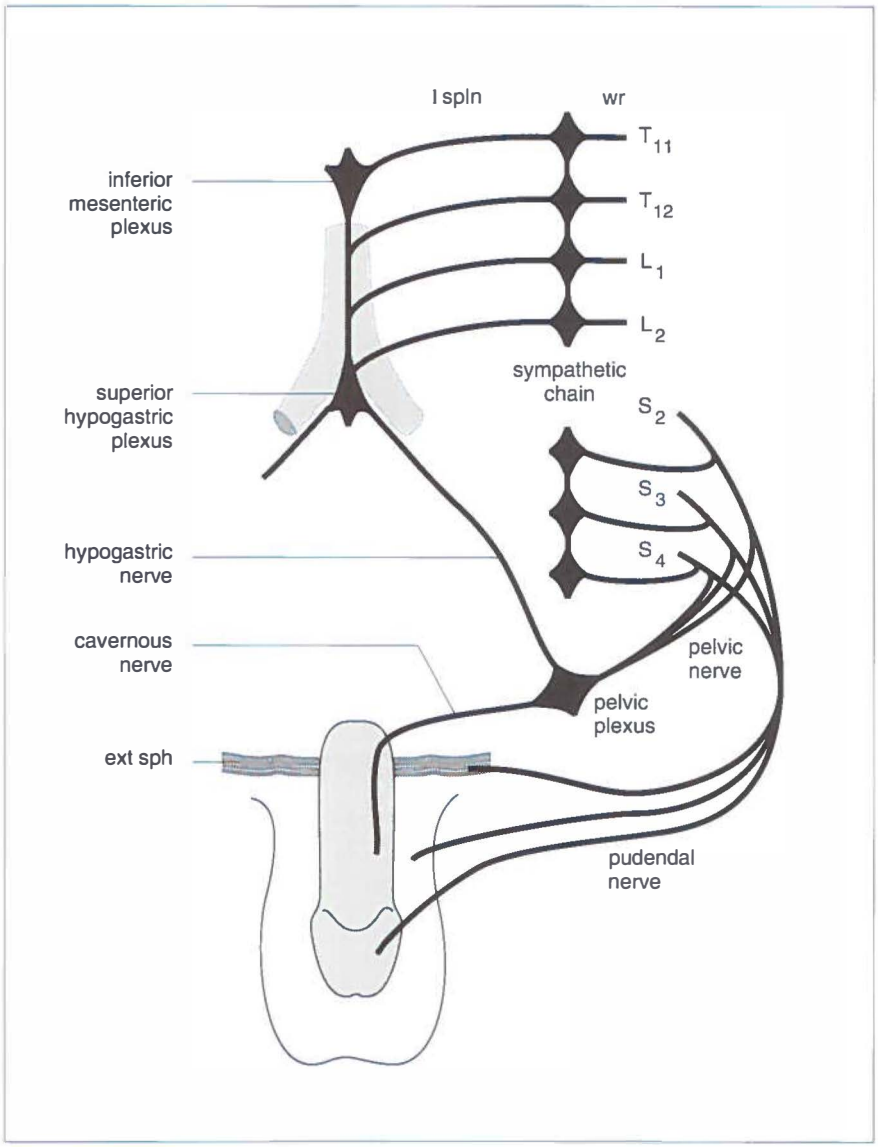

Figure 3 Diagrammatic drawing showing the nerve supply of the penis

as well as numerous vascular and lymphatic vessels obscure this plexus making its intraoperative identification difficult. The pelvic plexus provides visceral branches that innervate the bladder, ureter, seminal vesicles, prostate, rectum, urethra and corpora cavernosa. Moreover, autonomic fibers innervate the vessels in the pelvic area. The branches to the corpora cavernosa, the cavernous nerves, are located

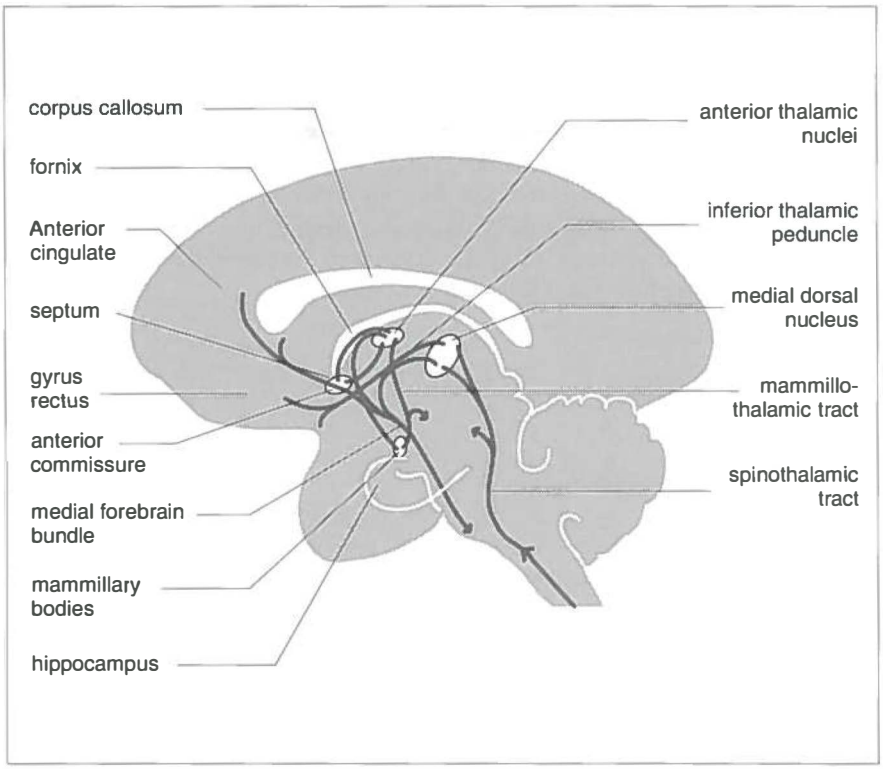

Figure 4 Anatomic diagram of cerebral circuits involved in elemental sexual functions

in the pelvic fascia before it fuses with the prostatic capsule and then travel along the posterolateral aspect of the prostate. At the prostatic apex the nerves are only a few millimeters from the urethral lumen. In cross sections of the membranous urethra, the cavernous nerves can be seen at the 3 and 9 o'clock positions. Distal to the membranous urethra, some fibers penetrate the tunica albuginea of the corpus spongiosum while the remaining fibers, lying at the 1 and 11 o'clock positions, enter the penile crura along with terminal branches of the pudendal artery. The course of the cavernous nerves is clinically important since bulbous or membranous urethral injury as well as prostatic, rectal, or bladder surgery can disrupt the nerves and may result in impairment of erectile function.

The sensory innervation to the penis is almost exclusively through the dorsal nerve of the penis, which is a branch of the pudendal nerve. The pudendal nerve is formed by the anterior branches of S2 to S4. Autonomic fibers run along with the pudendal nerve, parasympathetic as well sympathetic. The latter join the anterior branches of S2 to S4 by means of rami communicantes from the ganglia in the sacral sympathetic chain.[2] The pudendal nerve does not contribute to the pelvic plexus but

leaves the pelvis through the lower part of the greater sciatic foramen, crosses the spine of the ischium and re-enters the pelvis through the lesser sciatic foramen. Once in the ischiorectal fossa, the pudendal nerve gives off its first branch, known as the inferior rectal nerve, and subsequently divides into the perineal nerve and dorsal nerve of the penis. The dorsal nerve accompanies the internal pudendal artery along the ramus of the ischium and then runs forward along the margin of the inferior ramus of the penis, lying between the superficial and deep layers of fascia of the urogenital diaphragm. After piercing the superficial fascia it gives branches to the corpora cavernosa and runs along the dorsum of the penis, distributing sensory fibers to the skin, and terminates at the glans penis.

C. HEMODYNAMICS

C_1 The role of the arterial system

Hemodynamic studies show a six- to eightfold increase of flow in the internal pudendal artery after stimulation of the cavernous nerve in both systolic and diastolic phases.[3,4] Since this increase in blood flow is not associated with any significant change in systemic blood pressure, it can only be explained by a marked reduction in peripheral resistance of the penile arterioles and sinusoids. In the flaccid state the penile arterioles and the smooth muscles of the sinusoids are contracted due to a tonic discharge from sympathetic nerve fibers. This causes a maximal resistance against arterial flow, allowing only a small amount of blood to enter the corpora for nutritional purposes. Immediately before erection a release of neurotransmitters causes relaxation of the arterioles and smooth muscles of the sinusoids. This relaxation together with a continuous arterial filling promotes a maximal expansion of the sinusoids. During erection the pressure within the corpus spongiosum and glans penis remains lower than the intracavernous pressure (see B_2) and a considerable amount of blood continues to flow into their less-resistant sinusoids. Thus, in erection, flow through the internal pudendal artery remains higher than in the flaccid state.

C_2 The role of the venous system

The small veins draining the corpora cavernosa course between the sinusoidal wall and the tunica albuginea for some distance before their exit as emissary veins.[5] When the sinusoids are contracted (in the flaccid state) these venous channels are wide open and drain freely into the superficial penile veins. During erection the distension of the sinusoidal spaces is limited by the relatively indistensible tunica albuginea and the small veins are compressed between the sinusoids. At full erection the sinusoids expand further and compress the intermediary veins between the sinusoidal wall and the tunica albuginea. Thirdly the stretching of the tunica

compresses the emissary veins (figure 2).

The drainage of the glans penis and corpus spongiosum is different. The corpus spongiosum connects distally to the glans and has scanty emissary veins and subtunical veins similar to those of the corpora cavernosa. Functionally, because the corpus spongiosum communicates freely with the glans and has a thinner tunica albuginea, it is compressible and the pressure is lower during erection. Because there is no barrier between the glans penis and the deep dorsal vein (the glans has no tunica albuginea), the glans functions as an arteriovenous fistula during erection. The pressure is about half of the pressure of the corpora cavernosa. This is well suited to its physiologic role as a shock absorber to protect the cervix from the impact of the rigid corpora cavernosa.

C_3 The role of the perineal muscles

The role of the perineal muscles is not clearly understood. Animal studies have shown activation of the ischiocavernous and bulbocavernous muscles during coitus.[6,7] Their electromyographic activity correlates with peaks in the intracavernous pressure, which can reach values of a ten-fold to the arterial pressure. Lue and coworkers found the intracavernous pressure to rise to about 20 mm Hg below the systolic pressure after stimulation of the cavernous (autonomic) nerve alone.[3] When pudendal nerve (somatic) stimulation was added, the intracavernous pressure rose well above the systolic pressure. This suggests the importance of the perineal muscles to attain maximal penile rigidity. Lue postulated that once penile tumescence is achieved by autonomic neural stimulation a bulbocavernous reflex is triggered.[8] Contraction of the bulbo- and ischiocavernous muscles then compresses the proximal parts of the corpora cavernosa and raises the intracavernous pressure above the systolic blood pressure, resulting in the rigidity which can be reached during masturbation or intercourse. Contraction of these muscles also compromises the lumen of the deep dorsal vein and contributes to increased pressure and engorgement of the glans penis.

D. NEURAL CONTROL

D_1 Central pathways

The entire process of erection in humans is under considerable control by higher centres. In various species supraspinal mechanisms involved in erection have been identified using lesioning and electrical- or chemical stimulation techniques. Extensive studies in monkeys and rats indicate the hypothalamic and limbic pathways to play a key role in psychogenic erectile mechanisms and the medial preoptic-anterior hypothalamic area to be an important integration centre[9-14] (figure 3). Efferent pathways from the medial preoptic area enter the medial forebrain bun-

dle and then pass caudally into the midbrain tegmental region near the lateral part of the substantia nigra.[12,15] In monkeys the efferent pathway for eliciting erection runs caudal to the midbrain into the ventrolateral part of the pons and medulla.[12] Neuroanatomical studies have demonstrated direct projections from a number of hypothalamic nuclei to the spinal cord, some of which terminate in the lumbosacral autonomic centres involved in erectile function.[16,17] Within the spinal cord the descending tracts for erection lie within the dorsolateral funiculus. The anterolateral and dorsal ascending tracts are involved in transmitting afferent information from the urogenital organs to the brain.[18-20]

In contrast to the well-established role of the hypothalamospinal autonomic pathways in mediating sexual responses, the function of higher centres in the brain is less clear. MacLean and co-workers identified in monkeys three cortical-subcortical divisions of the limbic system with a role in the control of penile erection: a) the gyrus rectus, the medial dorsal nucleus of the thalamus, and regions of their known connections, b) the cingulate gyrus, mammillary bodies, and anterior thalamus, c) the hippocampus and hippocampal projections to the septum (figure 3).[14,15]

Although electrical stimulation at some of these sites elicited penile erection alone, many sites responded also with other autonomic effects such as voiding and a change in pulse rate, indicating that sexual pathways overlap with other autonomic control systems. This is no surprise since we know that sexual arousal and intercourse are associated with a variety of autonomic changes together with erection.[14,17]

Since lesions of the pyriform cortex and the adjacent amygdaloid complex may produce hypersexuality and frequent penile erections (the Klüver-Bucy syndrome), this region of the brain may well inhibit sexual function.[10,15,21] It is obvious that several central brain systems modulate erection since we know that a variety of stimuli (i.e., visual, olfactory, auditory, imaginative) can elicit erection. The Klüver-Bucy syndrome has, in its pure form, only been observed in monkeys. In humans bilateral lesions of certain temporal lobe areas may produce hypersexuality, but always accompanied by an amnesic defect, aphasia, bulimia or dementia.

D_2 Peripheral pathways

The peripheral afferent and efferent pathways use two pathways, a) pudendal nerve and b) cavernous nerve.

a. The pudendal nerve arising from sacral segments S2–S4 is a mixed motor-sensory nerve providing motor innervation to the perineal striated muscles and sensory innervation to the penile and scrotal skin. It also provides innervation of the penile urethra, the corpus spongiosum and the glans penis.[22] The dorsal nerve of the penis is the terminal deeper branch of the pudendal nerve. It has nonspecific free spray nerve endings which serve as sensory receptors in the glans and penile skin. Autonomic fibers run along with the pudendal nerve, parasympathetic as well as sympathetic.

b. The preganglionic cavernous nerve constitutes the major motor input to the corpora cavernosa and corpus spongiosum, and synapses with more distal neurons, which neurotransmitter(s) are not exactly known yet. The cavernous nerves contain parasympathetic, sympathetic and somatic axons. Two putative transmitter mechanisms, cholinergic and peptidergic are currently the subject of many studies. The cavernous nerve arises from the pelvis plexus. Parasympathetic nerves enter this plexus via the pelvic nerve, which was named the nervus erigentes by Eckhardt in 1863.[23] The sympathetic contribution to the pelvic plexus comes mainly via the hypogastric nerve (see A5).

Attention to the sympathetic nervous system was first drawn when following removal of all parasympathetic innervation in male cats (by ablation of the entire sacral spinal cord), full erections could still be observed when estrous female cats were present. In these animals spinal cord transsection above the thoracolumbar sympathetic outflow abolished erectile function completely, suggesting a significant role in erection for the thoracolumbar sympathetic outflow.[24] However, it does not appear that, in the neurologically intact man, the thoracolumbar sympathetic outflow plays a significant role in initiating or maintaining penile erection. A model for bilateral ablation of these tracts is provided by radical retroperitoneal node dissection for testis tumor. In that situation, emission and ejaculation may be abolished, thereby proving that sympathetic outflow has been ablated, and nevertheless there is no probably effect on erectile function.[25]

E. ANDROGEN CONTROL

A reduction in androgen levels after castration or as a consequence of endocrine disorders can lead to loss of libido and reduced erectile and ejaculatory function.[9,26,27] In many patients these effects may be preserved or restored by systemic administration of testosterone but also by testosterone injection into the brain sites that control erection.[9] Radiographic studies have shown that these sites also accumulate large quantities of testosterone after systemic administration.[28-30] Thus both nerve cells and peripheral effector organs are targets for hormonal modulation.

Double-blind controlled studies of testosterone suppletion in hypogonadal individuals have provided a key to the apparent contradiction between data which suggest that erection is testosterone dependent and the observation that erectile function is sometimes retained after castration.[31-33] In castrated individuals testosterone suppletion may result in recrudescence of libido and restoration of ejaculation. The situation with regard to erectile functioning is however more complex. Erections during sleep, spontaneous daytime erections, and erections in response to erotic stimuli may be distinguished. Spontaneous erections, nocturnal and diurnal, were markedly suppressed in hypogonadism and could be restored by androgen suppletion. In contrast, erections as a response to erotic films continued, with or without androgen suppletion, in spite of the marked effects of testosterone re-

placement on sexual interest and behaviour.[34,35] So the central processes that lead to spontaneous erections are testosterone dependent, while the mechanisms leading to erection in response to a certain type of external erotic stimuli remain intact despite androgen deficiency.

Although the importance of testosterone for a normal sexual life is established, the amount required for optimal function is still unknown and may be individually dependent. Undoubtedly there is an overlap in androgens levels between normal and impotent males.

F. CONCLUSION

Penile erection is a complex physiologic response depending upon the integration of vascular, neurologic and endocrine mechanisms. Although many aspects of the neurohumoral control of erection are still unknown, it is clear that erectile responses can be triggered by a variety of psychogenic and reflexogenic stimuli. They produce a neurally mediated dilatation of the penile blood vessels leading to an increase in blood flow, relaxation of smooth muscle cells of the sinusoidal spaces in the corpora cavernosa and reduction of venous drainage by the specific anatomy of the different parts of the venous system.

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CHAPTER 3

DIAGNOSIS AND TREATMENT OF ERECTILE DYSFUNCTION

A INTRODUCTION

As recently as 1960, impotence in the absence of demonstrable gross neurologic, anatomic, vascular, or hormonal abnormalities would have been diagnosed as of psychogenic origin. Textbooks cited a 90 percent incidence of psychogenic origin and only a 10 percent incidence of organic impotence.[1]

In the ensuing 30 years however, diagnostic tools allowing a better determination of the cause of impotence with a high accuracy, became available. The true incidence of organic impotence is nowadays considered to range from 30 to 50 percent, depending on the group of patients studied.[2]

Medical technology today has advanced sufficiently to accommodate most patients who seek treatment for organic impotence. The present therapeutic modalities guarantee a sufficient penile rigidity for vaginal intromission. However, both medical and surgical treatments go along with unfavourable side effects, so the urologist must resist the temptation to treat without a proper diagnostic evaluation. With the plethore of diagnostic tests available today, he must choose among a confusing array of more or less expensive and sometimes rather esoteric tests, many of which are probably not necessary to determine the etiology of impotence in the majority of patients. In this chapter diagnostic procedures and the medical and surgical modalities for the treatment of impotence will be discussed.

B HISTORY

The medical history is extremely important as with any disease. The precise sexual problem must be defined. At the end of the interview, the physician should be informed precisely about the patient's actual problem and its severity. Men frequently refer to problems of libido, premature ejaculation, retarded ejaculation, or lengthy post-ejaculatory refractory periods as impotence. To limit errors of omission, each patient should be asked to answer the same battery of questions (table I). The general medical and surgical history is taken to find factors that might have an effect upon the anatomic, vascular, neurologic, hormonal or psychological aspects of erectile function. Any drug, whether legal or illicit, may effect vascular or neurologic mechanisms, alcohol, marijuana and tobacco must be considered in this respect. In table II various drugs that can effect sexual function are listed. Due to our current incomplete knowledge of normal sexual function, the possibility of other, yet unknown, mechanisms of drug interference with sexual function must be recognized. Any agent that alters the hormonal balance, the somatic or autonomic neurotransmission or the vascular flow may also alter erectile function. The history of sexual dysfunction following a major surgical procedure often establishes a clear organic association.

The onset and consistency of the erectile dysfunction are important. Impotence secondary to progressive organic disease generally has a pattern of gradual deterioration. Psychogenic impotence is usually associated with normal erections in cer-

Table I Standardized Questionnaire for Preliminary Assessment of Impotence

Chief complaint

Accurate description of erectile abnormality

- Problem initiating or maintaining erection
- Duration of erection
  - Erection lost before or during coitus
  - Loss of erection associated with ejaculation
  - Positional differences (missionary vs. side-to-side, upright, or female-superior)

Duration of problem

- Intermittent or situational
- Traumatic event at onset (e.g., death of family member, widower's syndrome, accident, loss of job)

Change in erectile deficit (plateauing, worsening, improving)

History of premature ejaculation

History of penile or pelvic trauma

Penis straight or curved when erect

Morning, night, or masturbatory erections

Libidinal status

Who initiated consult: patient or partner

Cigarette smoking; marijuana

History of alcohol or other drug abuse (how much, how long, medication, dosage, relation to onset of symptoms)

Personal or family history of diabetes

History of hypertension

History of major illness or surgery (TUR-prostate, vascular surgery, HNP-operation etc.)

Paresthesias (including change in penile sensation)

Change in strength, gait, loss of balance

Sympoms of claudication; angina pectoris

GU history, particularly pain in perineum or testes with ejaculation

Back pain or injury

Patient's perception of cause of problem

Patient's goal in seeking appointment

Table II Drugs That Can Affect Sexual Function

Psychotropic drugs-antianxiety
- Diazepam
- Oxazepam
- Chlordiazepoxide

Psychotropic drugs-tranquilizers
- Phenothiazines
- Butyrophenones
- Thioxanthenes

Psychotropic drugs- antidepressants
- Tricyclics
- Monoamine oxidase inhibitors
- Lithium carbonate

Anticholinergic drugs
- Belladonna alkaloids
- Antispasmodics
- Anti-Parkinson drugs
- Antihistamines
- Muscle Relaxants
- Antiarrhythmic drugs

Anthiypertensive drugs
- Diuretics
- Vasodilators
- Central sympatholytics
- Neurotransmitter depletion

Miscellaneous drugs
- Cimetidine
- Clofibrate
- Digoxin
- Estrogens
- Glucocorticiods
- Immunosuppressive agents
- Indocin
- Levodopa
- Methysergide
- Metoclopramide
- Progestins
- Cocaine
- Alcohol
- Marijuana

Table III Components of Physical Examination of the Impotent Patient

observation	findings and problem suggested
Patient gait	Neurologic disease; effects of medication, drugs
Appearance of skin	Endocrine deficits Nicotine staining (vascular disease)
Blood pressure	Smal-vessel disease
Head and neck	Carotid bruit (atheroscerosis) Peripheral fields Pituitary tumor Extraocular movement, retinopathy Thyroid enlargement
Thorax	Gynecomastia (increased estrogens) Cardiomegaly, arrhythmias, rales
Abdomen	Liver enlargement, aortic aneurysm
Penis	Fibrosis, cancer, phimosis, urethral discharge, sensory deficit
Scrotal contents	Epididymal pain, testicular atrophy
Prostate	Cancer, inflammation
Rectum	Cancer
Vascular	Femoral and pedal pulses

tain circumstances, (e.g. masturbation) and flaccidity in other circumstances (e.g. intercourse).

C PHYSICAL EXAMINATION

The aim of the initial physical examination is to detect anatomic, vascular, neurologic or hormonal factors that may be associated with the erectile dysfunction. In table III some conditions that might be causative are listed. Neurologic examination is necessary to document the presence, location, and completeness of a lesion. Special attention should be paid to symptoms of pyramidal tract dysfunction, somatic or autonomic polyneuropathy, and lesions of the conus medullaris and cauda equina. Therefore assessment of reflexes, muscle power and sensory functions in the lower limbs and perineal region is mandatory. Observation of resting tone, voluntary control and the reaction on coughing and straining of the external anal sphincter gives information about the integrity of the somatic central and peripheral motor nerve fibers. The integrity of the sacral reflex arc may be assessed

by the bulbocavernosus reflex and the anal reflex. Classically the bulbocavernosus reflex is elicited by sudden manual compression of the glans penis and palpation of the perineum or anus for the reflex contraction. This reflex is clinically detectable in 70 percent of normal men.[3] The anal reflex is elicited by pin-prick or scratching of the skin just outside the anocutaneous margin. The reflex answer is a brief visible or palpable contraction of the anal ring. Absence of these reflexes may indicate an interruption of the sacral segmental reflex arc. The lesion can be located in the pudendal nerve, which contains both afferent and efferent fibers, or in the conus medullaris. The sensory status of the penis and perineal region can be obtained by means of testing pain, temperature and light touch sense.

D TESTS

D_1 To determine the presence of a rigid erection

A sexually stimulating movie has been used to observe whether the patient can obtain a rigid erectile response or not. The test is most accurate when a longlasting (more than 5 minutes) rigid erection is observed. The inability to achieve an erection in such a way is however meaningless while some patients may be embarrassed by such a test.

Recognition that erections occur during rapid eye movement (REM) sleep episodes was first reported in 1944 by Ohlmeyer.[4] In 1965 the use of nocturnal penile tumescence monitoring (NPT) as a test for erectile dysfunction was suggested.[5] The working assumption was that these nocturnal erections would not be affected by neurosis or sexual satiation, but were vulnerable to the same physiologic or anatomical problems that might prevent or inhibit erections while the patient was awake. If a NPT test showed adequate erections the patient was capable of erection, if NPT was deficient, the dysfunction had an organic basis regardless of the patient's psychological condition. There are however three pitfalls in interpreting the results of NPT-monitoring.

The first is that not all devices measure penile tumescence *and* rigidity. The recording of changes only in the circumference of the penis is not adequate to assess rigidity, and so the capability of coitus. In that case an independent observer must be present to estimate the hardness or buckling pressure of the penis.

The second is that NPT monitoring is based on the assumption that men normally have four or five erections per night each of 10 to 15 minutes' duration. However it has been reported that in 20 percent of young, normally potent men the NPT tests were not normal when studied in a sleep laboratory setting.[6] In fact there is no single group of NPT values (standards and norms) that can be applied to the entire male population. Looking at the overall picture through a man's life, it has been

found that from age three until quite late in life, NPT episodes gradually decrease in frequency and are of shorter duration.[7] In pubescent boys more than six erections occur each night with more than 2.5 hrs (40%) of sleep time spent with erection. This activity slowly declines to a level of three to four erections per night with a duration of 20 percent of total sleep time at the age of 60.

The third pitfall is the presence of sleep disorders.[8] The anxiety of the testing situation may result in transient insomnia and fragmented sleep, especially during the first night of testing. Rapid eye movement sleep may be delayed or suppressed by a variety of medications. Sleep may also be disrupted by other disorders such as sleep apnea and periodic leg movements in sleep (nocturnal myoclonus). Some authors therefore feel that NPT studies need to be performed in a sleep laboratory setting during at least 2 consecutive nights.[9]

In short, NPT is a naturally occurring, non-sexually stimulated phenomenon the mechanism of which is presumed to be similar to that of the erotic erection. It most often occurs around REM sleep but may also be present during non-REM sleep. Normal NPT in a person with sexual dysfunction would suggest psychogenic impotence, and an abnormal recording would suggest organic impotence. NPT-monitoring should be used with the reservation that absence of nocturnal erections with rigidity sufficient for vaginal intromission is found frequently in normal males, even if registration is performed for several nights.[10] Despite the forementioned pitfalls NPT-monitoring remains an adequate non-invasive examination to differentiate organic from psychogenic impotence. The need to measure rigidity concurrently with tumescence is well known, so monitoring with the RigiScan® or Surgitek-ART-1000®, which measure both parameters, is the procedure of choice when evaluating NPT. These devices can also be used for real-time monitoring in situations where erections obtained with sexual stimulation need to be documented or the efficacy of intracavernous injections with vasoactive drugs needs to be tested.

D_2 To determine the adequacy of penile blood circulation

Several invasive and noninvasive techniques are available to determine the status of penile blood circulation. These tests include intracavernous injection of vasoactive agents such as papaverine, measurement of penile artery pressure, pulsed Doppler assessment of flow in the penile arteries, selective pudendal angiography and the combination of cavernosometry and -graphy.

Intracavernous injection of several types of drugs may cause relaxation of the smooth muscles of the corpora resulting in a pharmacologic erection. Papaverine was used at first and still is the most frequently applied drug for this purpose. When injected into the corpora of a man with normal erectile function, the response will be lengthening of the penis and tumescence followed by rigidity if he is not excessively anxious. Some authors have suggested the use of papaverine injection

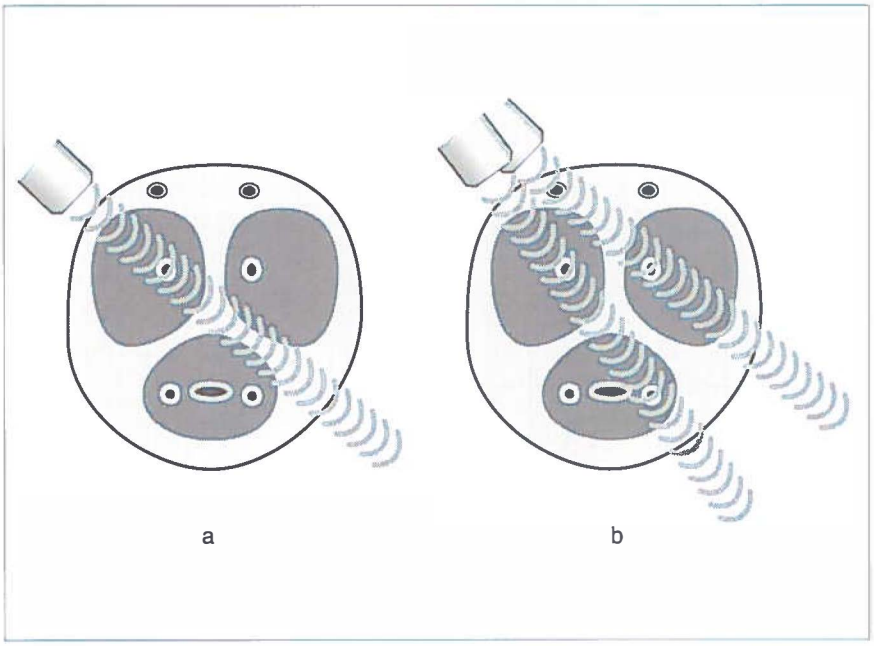

Figure 1 Schematic representations of Doppler pathways and penile arteries.
a. Path of Doppler beam required to isolate single cavernous artery
b. Multiple penile arteries can be sampled by single transducer beam. Without direct visualization and sampling of cavernous artery, dorsal or urethral artery signal could be sampled unknowingly.

to discriminate between organic disease, vascular insuffiency or abnormal corporal drainage, and psychogenic failure, in the assumption that a rigid erection after papaverine injection eliminates arterial insuffiency.[11] However, if erection is not achieved, the result is to be considered inconclusive and repetition of papaverine injection at another time is mandatory. Perhaps an increased adrenergic tone resulting from emotional stress present at the time of the test can explain the lack of response in psychogenically impotent patients. If negative for the second time, NPT testing and/or dynamic cavernosography should be done for confirmation.[12]

The standard method of measuring penile arterial pressure employs a 8–10 mHz Doppler ultrasonic probe and an occlusive 2.5–3 cm wide blood pressure cuff around the base of the penis. Then simultaneously measured brachial artery pressure is compared with either the highest penile pressure or the mean pressure of all vessels where systolic pressure can be detected. A score, penile brachial index (PBI), is calculated as the ratio of the systolic penile artery pressure to the systolic brachial artery pressure. A ratio of less than 0, 6 is thought to be diagnostic of vasculogenic erectile dysfunction.[13] The accuracy of PBI is reduced by variation either in penile artery supply or in the size of the penis. Also there may be an arterial spasm, a lack

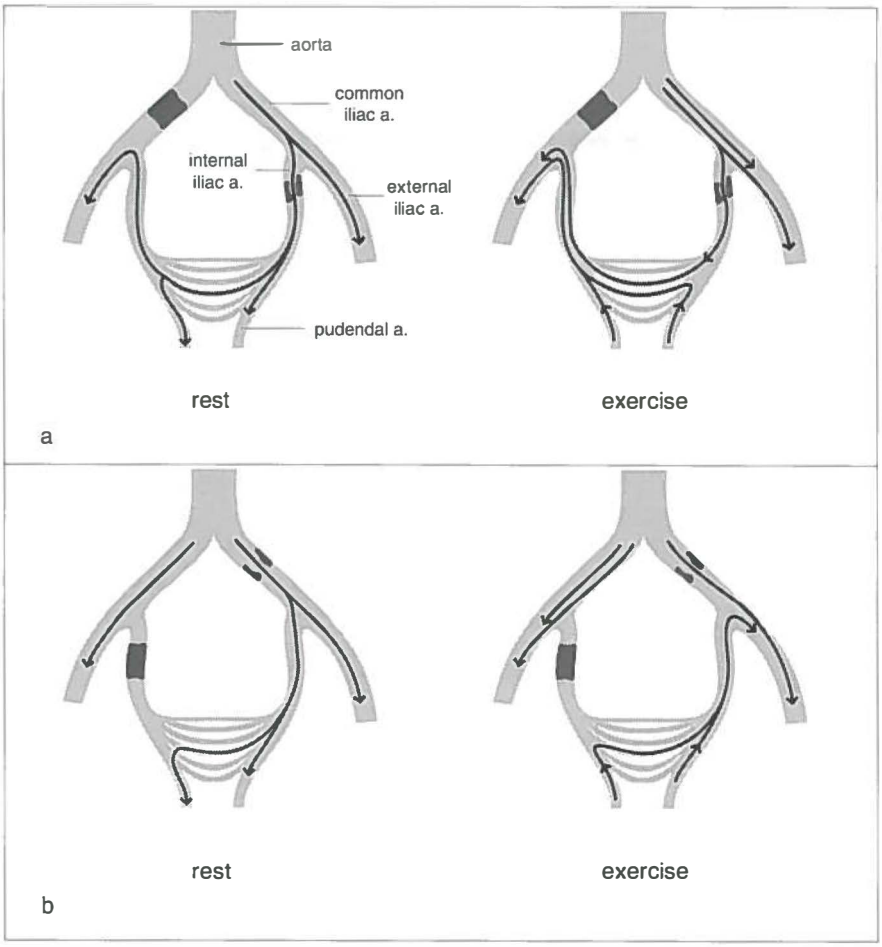

Figure 2 Schematic arteriograms demonstrate pelvic steal symdrome
a. Obstruction of the right common iliac artery with reversal of the flow in the pudendal arteries during exercise at intercourse.
b. Obstruction of the right internal iliac artery showing the same phenomenon.

of significant pressure drop with small vessel disease, or even uncertainty whether the cavernous or dorsal penile artery is being auscultated at all (figure 1).[14]

Patients with a problem in maintenance of erection, especially during intercourse, may have a "steal phenomenon" leading to insufficient flow to the penile arteries because the blood flow is preferentially directed towards the muscles in buttocks and legs. This steal phenomenon may be due to obstruction of the common or internal iliac artery (figure 2). A test for pelvic steal may be conducted by measuring the penile pressure after pelvic exercise. A drop of 0.15 or more in the penile brachial

index (PBI) is considered indicative of a vascular steal producing a decreased blood flow to the penis.[15]

Today, duplex scanning, performed after induction of maximal penile circulation by intracavernous pharmacostimulation has gained general acceptance as the standard in the evaluation of penile circulation. It has replaced the measurement of penile arterial blood pressure in the initial workup of a patient with erectile dysfunction. Peak flow velocity, acceleration, resistance index, dilatation of cavernous artery, volume increase of cavernous body and inducibility of erection are commonly measured parameters.[16] However, true normal values have not been determined yet. Therefore the finding of abnormalities by duplex scanning calls for independent testing by NPT monitoring to confirm arterial insuffiency as the cause of erectile failure.

Invasive vascular imaging techniques aim to diagnose arterial insufficiency (pudendal arteriography) and venous vascular insufficiency (cavernosography). The indication for selective pudendal angiography remains unclear. The procedure itself is not without risk. Intima dissection of the internal iliac artery is the most feared complication. Therefore it is rational to reserve selective pudendal arteriography only for patients with documented evidence of vasculogenic impotence who are considered candidates for a vascular bypass procedure. Other large-vessel procedures or percutaneous angioplasties might be considered also.

The second invasive vascular test to be considered is dynamic infusion cavernosometry and -graphy. Patients complaining about the inability to maintain an erection, who have adequate arterial inflow at duplex scanning after intracavernous pharmacostimulation, may benefit from this procedure. Initially, this study was performed with the infusion of saline intracavernously at increasing rates while pressure was recorded. If more than 160 ml/minute of saline was required to produce an erection, abnormal venous leakage was supposed to be present.[17] No intracavernous vasoactive drugs were used. Recently, it became clear that a more appropriate way to perform cavernosometry and -graphy is following the intracavernous injection of a vasoactive agent.[18] The American Society for the Study of Impotence has determined that a significant cavernous-venous leak should be diagnosed by either maintenance flow rate or by dynamic infusion cavernosometry and cavernosography[19]: 'If the maintenance flow rate 10 minutes after 45 to 60 mg of papaverine (or 10 μg of prostaglandine E1) injected intracavernously is greater than 30 ml/min to maintain intracavernous pressure greater than 90 mm Hg or to produce a fully rigid erection, abnormal venous leakage is assumed. Alternatively, when using only infusion cavernosography and cavernosometry, if the intracavernous pressure decreases from 150 mm Hg to less than 100 mm Hg in 30 seconds, or if the intracavernous pressure is less than 60 mm Hg at 5 minutes regardless of the initial intracavernous pressure, a venous leak likewise is diagnosed.'

Until 1990 there is no worldwide consensus on the optimal method to perform

cavernosometry and cavernosography.[20] Important unanswered questions remain. Can venous leakage be demonstrated in normal, potent males? Because a netto inflow of blood occurs during erection, some degree of 'venous leakage' must normally occur. If some degree of venous leakage always occurs, what separates normal from abnormal states? No convincing data have yet been presented describing the results of cavernosometry and -graphy in potent males of various age groups.

D_3 To determine the hormonal status

Patients reporting a diminished desire, with or without erectile failure, may have a reduction of plasma testosterone or an elevation of prolactine. The diagnosis can be made with a simple blood test. Patients with a diminished or low-normal testosterone level should have a repeat testosterone test accompanied by FSH and LH determinations to look for possible hormonal dysfunction. If repeat testosterone levels remain low and gonadotropin levels are not sufficiently elevated, the patient should be referred to an endocrinologist for evaluation of hypogonadotropic hypogonadism. If there is a defect at testicular level, gonadotropins will be elevated. It is the characteristic response of an intact hypothalamic-pituitary unit to testicular failure. Androgen substitution will only be helpful if the serum testosterone level is below the physiological range.

The causes of an elevation in serum prolactine levels are numerous but most frequently they include side effects from medication, chronic renal failure or the presence of a prolactinoma.[21] Drug induced hyperprolactinemia rarely is the only cause for erectile dysfunction.

Although thyroid dysfunction generally is not considered to cause impotence, hyper- and hypothyroidism have been associated with erectile dysfunction. Both loss of libido and decreased potency were noted in a study of hyperthyroid men.[22] An elevated baseline serum testosterone may be considered a biochemical marker for possible occult hyperthyroidism in impotent men.[23] This finding is related to increased sex hormone binding globulin, which is secondary to excess levels of endogenous thyroid hormone.[24] While diabetes mellitus may be defined broadly as an endocrinologic cause of erectile dysfunction, impotence in these patients is owing to neurogenic and/or vascular factors. Detailed studies of the hypothalamic pituitary gonadal axis in impotent diabetic men showed no significant difference from the findings in diabetics without impotence, normal controls or nondiabetics with impotence.[25]

In impotent men a cost-effective screening for hormonal dysfunction includes a careful history, physical examination and determination of serum testosterone level. A more complete hormonal investigation does not increase the diagnostic accuracy significantly and should be reserved for patients in whom there is clinical evidence of hypogonadism on physical examination or a decreased serum testosterone level.[26]

D_4 To determine the adequacy of penile innervation

Historically neurogenic factors have been felt to be the sole or major contributing factor in only 10 to 15 percent of all organically impotent men.[27] The neurologic evaluation of the impotent man serves two aims. First, to identify a neurologic component as contributing to or causing the erectile impairment. And second to identify the nature and location of the underlying neuropathology. The somatic afferent pathway may be evaluated by penile biothesiometry and dorsal nerve somatosensory evoked potential tests.[28,29] Information about the autonomic afferent fibers (in the pelvic nerve) can be obtained by the vesico-anal-reflex. The somatic efferent pathway to the perineal muscles can be assessed by the bulbocavernosus reflex and by means of electrical (and/or magnetic) brain- and spinal cord stimulation. The autonomic efferent pathway can at present only be evaluated indirectly using the results of intracavernous injection of a vasoactive drug.

$D_{4.1}$ Afferent pathway testing

The vibration perception threshold of the skin of the penis may be tested by penile biothesiometry. This proved to be an excellent screening evaluation to assess for an abnormality within the penile sensory afferent pathway.[28]

A biothesiometer is an electromagnetic device, with the size and weight of a pocket dictaphone, which provides a vibration stimulus through a 1 cm-wide tactor at a fixed frequency but variable amplitude. To determine penile vibration perception threshold, the tactor is applied first to a reference location such as the right and the left pulp areas of the index fingers. The amplitude of vibration in each location is increased while the patient is asked to note the first perceived vibration stimulus. The test is repeated several times until a reproducible value is obtained. Also the amplitude of vibration may be decreased until the patient no longer feels a vibration stimulus. The amplitude value observed to represent the vibration perception threshold while the stimulus is decreasing from vibration to absence of vibration should be the same as the value observed while the stimulus is increasing from absence of vibration to perception of vibration.

Finally, the biothesiometric tactor is applied to the test sites, the right and left sides of the mid penile shaft and the glans penis. If the vibration perception on any of these test locations varies from the values identified on control sites, the following checks are made. The tactor is applied to the control site until the amplitude of vibration perception is appreciated. At this time the tactor is directly applied to the test site. If the patient acknowledges vibration, then the test values are repeated. If he does not acknowledge vibration perception at this amplitude, then the amplitude is increased until first perception is achieved.

Normal biothesiometric values are age-dependent, which may be explained by Pacinian corpuscle degeneration, collagen infiltration, and atrophy of the penile skin with increasing age.[30]

A more formal neurophysiologic assessment of the entire pudendal nerve afferent pathway may be obtained by somato-sensory evoked potential testing.[29] This evaluation involves electrical stimulation of the dorsal penile nerve in a manner analogous to that used in sacral evoked response testing. Instead of recording an electromyographic response, this study records the evoked potential (EP) waveforms overlying the sacral cord and cerebral cortex.

The central electric response to peripheral nerve stimulation has a very low amplitude which is even smaller than routine background activity. This low-amplitude potential, however, can be separated out from larger background waveform activity by means of an averaging technique, because it is generated from a specific central nervous system location and is time locked with the stimulus. The first recorded latency period is the time from stimulation to the first replicated spinal response (peripheral conduction time). The second period is from the time of stimulus to the first replicated cerebral response (total conduction time). The central conduction time is the difference between these two latency values. For correct interpretation these pudendal evoked potentials should be compared with tibial- and median nerve evoked potentials.

Somatosensory evoked potential testing is useful not as a routine diagnostic evaluation, but rather as an objective measurement of the presence, location, and nature of afferent penile sensory dysfunction especially in those patients with subtile abnormalities on neurologic screening with biothesiometry.

Information about the autonomic afferent fibres in the pelvic nerve can be obtained by the vesico-anal-reflex. Electrical stimuli applied to the bladder wall will result in afferent volleys, conducted to the sacral cord by afferent pelvic nerve fibres. After polysynaptic transmission in the conus medullaris this will result in a reflex motor response of the external anal sphincter mediated by the pudendal nerve.

$D_{4.2}$ Efferent pathway testing

There is yet no test that defines precisely the integrity of the numerous tracts which constitute the cortical-sacral efferent pathway to the penis. It has been proposed that NPT monitoring may assess this pathway partially. The exact neurologic pathways involved in rapid eye movement (REM) erection are not yet known. Although REM associated penile erection and erotic-associated erection may not be controlled by the same neurologic pathways, these pathways are probably closely related.

The integrity of the corticofugal descending motor pathways to the voluntarily innervated striated perineal muscles can be assessed by means of electrical (and/or magnetic) brain- and spinal cord stimulation.

An objective test to assess the integrity of the efferent autonomic pelvic cavernous nerve, such as the bethanechol supersensitivity test for the pelvic vesical nerve, is not yet available. However it has been observed that intracavernous injection of papaverine in patients with a spinal cord lesion results in a dramatic and

Table IV Treatment According to the Type of Erectile Impotence

Psychogenic	Psychosexual counseling Yohimbine? Intracavernous injection as an adjunct Vacuum constriction device Erection prosthesis (as a last resort)
Hormonal	Appropriate hormones Medication or surgery for prolactinoma
Neurogenic	Intracavernous injection Vacuum constriction device Erection prosthesis
Arterial	Intracavernous injection Vacuum constriction device Arterial surgery or balloon dilatation Erection prosthesis
Venous	Vacuum constriction device Intracavernous injection Venous surgery

sustained rise in intracavernous pressure.[31,32] It may reflect therefore a variant of denervation supersensitivity.

So practically a patient with erectile dysfunction, with normal vascular testing, an absent or abnormal nocturnal penile tumescence monitoring, and a supersensitive response to intracavernous injection of papaverine should be considered to have an efferent autonomic neuropathy as the cause of his neurogenic impotence.

D_5 To determine psychological causes

Paper and pencil tests, such as the Minnesota Multiphasic Personality Inventory and the Derogatis Sexual Functioning Inventory, are not useful in discriminating psychological from physical causes of erectile dysfunction.[33]

Separate private interviews of the patient and his sexual partner by an experienced sex therapist however have been particularly effective in establishing the diagnosis and the best plan of therapy.[34]

Recently Boyarsky and Lewis found that a practicing urologist with a properly trained nurse can form a dual (male, female) "sex therapy team".[35] Such a team would perfect sexual history-taking from both partners, provide a holistic approach to management, help to avoid certain misdiagnoses, and improve case selection for surgical therapy.

E TREATMENT

After a diagnosis is established, a plan of therapy must follow. The appropriateness of the different treatment options (including no treatment, sexual options, medical therapy, surgical procedures, and miscellaneous others) depends on the potential reversibility of the dysfunction and the choice of the patient. The different options will be discussed but certainly it is worthwhile to advise a ban on tobacco smoking and to convince the patient to stop smoking altogether. Our proposed treatment for various types of impotence is listed in table IV. One must realize that some patients are content to be informed about the etiology of their problem and do not wish a specific therapy.

F SEXUAL COUNSELING

A patient with organic erectile dysfunction together with his partner should be informed about the possibility of alternative methods of sexual interaction, with or without vaginal intromission. For some older patients, especially those with a chronic debilitating disease or men whose partner does not want them to submit to any type of intervention, other sexual options may fulfill their needs.

G MEDICAL THERAPY

G_1 Hormones

The goal of androgen substitution in impotence of endocrinologic origin is maintenance of the serum testosterone level in a physiologic range. A variety of androgen preparations are available. Unmodified crystalline testosterone, whether given parenterally or by mouth, is rapidly absorbed and degraded, so satisfactory blood levels are difficult to obtain. Effective androgen therapy therefore requires chemical modification of the testosterone structure. Preparations commonly in use have modifications by alkylation at the 17-alpha position, by esterification of the 17-beta-hydroxyl group, or modification of the ring structure.

The alkylated testosterone drugs have the advantage of oral administration, but the disadvantages of an erratic and poor absorption and the risk of hepatotoxicity.[36] Two commonly prescribed alkylated preparations are methyltestosterone and fluoxymesterone (Halotestin®).

By esterification of the 17-beta-hydroxyl group the testosterone is more soluble in fatty vehicles used for parenteral injection and allows for a slower release. Long-acting parenteral esters, such as testosterone cyprionate and enanthate, are the drugs of choice for substitution therapy in male hypogonadism. Testosterone propionate is a shorter-acting preparation that requires injection three times a week. It may be useful to initiate therapy in older individuals with borderline prostatism.

Any increase in prostatic obstructive symptoms will be quickly relieved upon stopping this drug. In the Netherlands a combination preparation of a short and long acting testerone ester (Testoviron-Depot®, Sustanon®) is usually prescribed for i.m. injection at 3 week intervals. Although most esters cannot be administered by mouth, two drugs, methenolone acetate and testosterone undecanoate (Andriol®), are both lipid-soluble compounds which are absorbed into the intestinal lymphatic system and may also be taken orally.[37] Hepatotoxic effects have been reported with the oral 17-alpha-alkylated androgens but not with the esterified compounds.[36,37] These effects may include elevations in hepatic enzymes and abnormal sulfobromophtalein retention. Although hepatoma and peliosis hepatis (blood-filled liver cysts) have also been listed as side effects, most individuals developing these complications have had a serious pre-existing medical condition such as aplastic anemia.[38]

Large doses of androgens stimulate erythropoietin production, so polycythemia may occur during this therapy. Testosterone may also cause feminization, due to a change in the testosterone: estradiol ratio. Since testosterone is aromatized peripherally to estradiol this may lead to gynecomastia, especially in patients with hepatic cirrhosis.[38]

Exogenous testosterone preparations may suppress gonadotropins and thereby indirectly spermatogenesis, resulting in a decrease in testicular size.[39] Weight gain secondary to sodium retention occurs occasionally and may be a significant problem in patients with congestive heart disease or with renal failure.[37] A consistent but minor complaint is that of increased oiliness of skin and acne. Testosterone replacement does not result in the development of prostatic cancer, but because this malignancy is androgen dependent, a patient with prostatic carcinoma should be excluded.

G_2 Yohimbine

Yohimbine is an indole alkaloid derived initially from the bark of the coryanthe johimbe tree. This alpha-2-adrenergic receptor antagonist has been promoted as a drug with the ability to enhance erection. However the response rate of organically impotent patients to Yohimbine is at best marginal.[40] Owing to its ease of oral administration, safety and modest effect it still is used in those patients who do not accept invasive methods.

G_3 Vasoactive intracavernous pharmacotherapy

A still increasing number of drugs are now available for intracavernous injection which cause penile rigidity in men with psychogenic and organic erectile dysfunction (table V).[41] Virag[42] and Brindley[43] demonstrated in their innovative work that papaverine hydrochloride, phenoxybenzamine and phentolamine can induce pe-

Table V Intracavernous Drugs that Promote Erection

Smooth muscle relaxants
Papaverine

Alpha-adrenergic blockers
Phentolamine
Phenoxybenzamine

Beta-adrenergic agonists
Isoxsuprine

Calcium channel blockers
Verapamil

Antidepressants
Trazodone
Chlorpromazine

Vasoactive intestinal polypeptide

Prostaglandin E1

nile erection when injected into the corpus cavernosum. Zorgniotti and Lefleur introduced the use of a mixture of papaverine hydrochloride and phentolamine for vasculogenic impotence[44], and Goldstein and colleagues advocate this drug mixture for neurogenic impotence.[45]

Papaverine is a potent, non specific smooth-muscle relaxant affecting muscle directly regardless of its innervation. The effects are maximal on smooth muscle of the vascular, bronchial, gastrointestinal, biliary, and urinary systems.[46] This spasmolytic action of papaverine involves inhibition of oxidative phosphorylation, blocking of cyclic adenosine monophosphate phosphodiesterase and interference with calcium flow during muscle contraction.[47] Papaverine has also an antinicotinic effect at the level of ganglionic transmission.[48]

Phentolamine induces smooth-muscle relaxation by blocking the alpha-adrenergic receptors on cell membranes.[49] By itself, phentolamine has a minimal effect on the venous outflow from the corpora cavernosa; however, it potentiates the action of papaverine when these drugs are administered concomitantly.[50]

Erotic stimulation can enhance the effect of intracavernous injection, whereas anxiety, lack of privacy, or a clinical environment can reduce the effect. In general, the penis becomes tumid within 5 to 10 minutes and rigid within 5 to 30 minutes after injection of the drug(s). The drugs do not effect the mechanism of orgasm or ejaculation.

Some groups of patients should be excluded from vasoactive intracavernous pharmacotherapy: Patients with significant venous leakage should not have this treatment modality since the leakage may result in rapid systemic absorption of

the drug and systemic effects. Patients with sickle-cell disease (priapism!) and patients who are susceptible to complications from a sudden hypotensive episode, such as with unstable cardiovascular disease or transient ischemic attacks, are no good candidates as well as patients who are on anticoagulant therapy. Intracavernous injection in men with psychogenic erectile dysfunction is problematic. It is tempting to offer this therapy to the man who wants a quick fix and refuses psychological treatment. However the possibility of permanent penile scarring as a result of priapism or local reaction to the needle or drug reinforces the concept that primary or simultaneous sex therapy should be offered as treatment.[51] Patients who like to start intracavernous self-injection therapy should get detailed information about possible complications and the possibility of long-term adverse effects of the treatment, although these are not yet known.

Complications include priapism, hematoma, cavernositis, inadvertent injection of the urethra, nodules and fibrosis. Hypotension, dizziness and hepatotoxicity are potential systemic side effects.

H SURGERY

H_1 Arterial revascularization surgery

Revascularization of the penis in arteriogenic impotence is now an accepted surgical procedure.[52] However, controversies still exist about the best way to achieve adequate arterial inflow to the corpora to restore erection. Direct corporal revascularization by anastomosis of the inferior epigastric artery to the corpus cavernosum or, alternatively a saphenous vein graft connected to the femoral artery, has been almost abandoned because of the poor long-term results, the high rate of thrombotic occlusion of the anastomosis, and the occasional development of a pulsatile priapism.[53,54]

An alternative method has been microsurgical anastomosis of the inferior epigastric artery to the dorsal artery of the penis. Such a procedure relies on the presumption that sufficient distal anastomotic branches between dorsal and cavernous artery do exist, and some good results have been reported.[55] Direct revascularization of the cavernous artery is theoretically more effective than that to the dorsal artery, because the former vessel is generally considered the most important way of arterial inflow to the penis during erection. However this type of anastomosis is technically demanding and not always possible, even in experienced and skilled hands.[56] Its location is deep in the areoalar tissue and its dissection is not easy. Furthermore, bleeding from the cavernotomy can obscure the view under the operating microscope, thus negating a perfect microvascular anastomosis. Finally one may have some concern about the fate of the epigastric artery running through a cavernotomy and then being embedded in potentially scarred tissue.

To overcome these difficulties Sharlip in 1984 described the possibility of anastomosing the inferior epigastric artery to the proximal stump of the transected dorsal

penile artery, so that the cavernous artery was revascularized in a retrograde manner through the common penile trunk.[57] Distal penile vascular supply is thought to be assured by anastomotic arcades from one side of the glans to the other. This operation is particularly suitable for patients with obstruction of the pudendal or common penile artery demonstrated at arteriography.

Hauri observed that the inferior epigastric artery anastomosis to the dorsal penile artery was often found thrombosed postoperatively.[58] To overcome this he fashions a longitudinal anastomosis between one of the dorsal penile arteries and the dorsal penile vein over 2 centimeters. The medial margins of these two penile vessels are interconnected and the remaining margins of the common arteriovenous lumen are anastomosed to the switched inferior epigastric artery. In 44 consecutive patients, Hauri identified an 89% success rate. Complications with this procedure have been minimal, including glans hyperemia and cavernous leakage.

In the presence of cavernosal artery occlusion, arterialization of a deep dorsal vein segment may be considered if retrograde flow through a deep dorsal vein segment into the corpora cavernosa can be established. The procedure is as follows[59]: The deep dorsal vein is identified at the base of the penis and a 3 to 4 cm long segment of vein including its emissary vein branches is temporarily isolated and occluded with vessel loops. This segment begins distally at approximately mid-shaft and extends proximally under the pubic symphysis to the mid-suspensory ligament. To establish the capability of retrograde arterial flow through the deep dorsal vein, one corpus cavernosum is first cannulated with a 19-gauge butterfly needle and free flow of cavernous blood is established. A dilute methylene blue solution is then injected into this isolated venous segment using a 25-gauge needle and the cavernous effluent is observed. When it turns blue, arterialization of the dorsal vein segment is performed using the inferior epigastric artery (or the ipsilateral dorsal artery) as the neo-arterial inflow source. Prior to performing the anastomosis, suture ligatures on the deep dorsal vein are placed, distally to insure against glans hypervascularization, and proximally to complete the isolated segment. In the event that retrograde flow cannot be established, one may opt for a direct fistula from the arterialized venous segment to the tunica corpus cavernosum by excision of a piece of the tunica albuginea.

The restoration of adequate erectile functioning with large vessel vascular reconstructive procedures or with transluminal angioplasty has been succesful in patients if the distal penile vasculature is relatively free of arterial occlusive disease. Unfortunately, the majority of patients with proximal arterial occlusive disease have been atherosclerotic in etiology and also have distal pathology in the hypogastric-cavernous arterial bed. This accounts for the relatively poor response of impotent patients to proximal vascular reconstructive procedures.[60]

H_2 Surgery for venous leak

Dissection and ligation of penile venous channels can restore or improve erection in selected patients.[61] There are few patients who have congenital or inflammatory-associated abnormal venous draining channels. These patients will demonstrate significant drainage on dynamic cavernosography by veins that usually drain into the external pudendal and femoral veins (normally the drainage of the corpora cavernosa occurs through the crural veins and the deep dorsal penile vein). These patients may describe life-long soft erections or may have Peyronie's disease. Only the former category may be expected to respond to removal of the abnormal veins.

An oblique infrapubic incision that extends in its lower margin around one side of the penis onto the scrotum is preferable since penile edema will be less likely because the lymphatics in this region are spared. By everting the penis into the incision veins of the whole shaft of the penis can be ligated. If the deep dorsal vein is a major source of efflux on dynamic cavernosography it is usually removed to the level of the suspensory ligament.

H_3 Erection prosthesis surgery

The use of a synthetic implant in the surgical treatment of erectile failure was first reported in 1952.[62] It revolutionized the therapeutic approach: the ability to resume coitus could be offered to patients with an organic erectile dysfunction. A recent study on long-term results of penile implants indicated that the return of a sense of masculinity to the impotent man was the most important effect. Less important was the type of prosthetic device. Nevertheless the sexual partners of men with an inflatable prosthesis tended to be more satisfied than the partners of men with a semirigid prosthesis.

Once the decision is made to use an implant the type of device must be chosen. The basic choice is between a semirigid or an inflatable one. It is preferable to make the decision after the different types have been shown and explained to the patient. The patient's sexual partner should always be involved. The mechanical failure rate of inflatable prostheses must be discussed.[63] The risk of postoperative infection can be reduced to less than 5 percent with meticulous surgical technique and pre- and intraoperative antibiotics.

I EXTERNAL DEVICES

Vacuum constriction devices are a nonsurgical, noninvasive alternative treatment for psychological and organic erectile dysfunction.[64] The method involves the placement of the penis in a tube and creation of a vacuum by suction using a hand driven pump (figure 3). Blood flow into the sinusoidal spaces is then facilitated by the lower pressure and a constricting band is placed at the penile base to trap the blood in the corpora. Problems with the use of the device include numbness caused

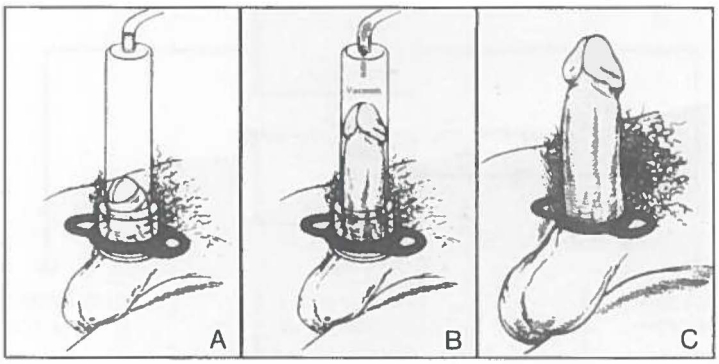

Figure 3 Vacuum assisted erection

by the tourniquet and the mechanical nature of erection. Up till now there are no studies about the effects of long-term use of this device on the penile tissue.

J CONCLUSION

The first step in the successful management of erectile dysfunction is proper identification of the cause. In the past most causes were thought to be psychogenic. However, recent advances in the understanding of the hemodynamics and neurophysiology of erection, as well as advances in diagnostic techniques, have made it clear that this is not true. Although the percentage of patients with psychogenic or organic impotence varies with the population under study, the overall feeling is that organic causes are more prevalent than previously had been assumed. In no way, however, should this minimize the importance of psychologic factors to erectile dysfunction. Organic causes are frequently aggravated by the psychologic overlay.

The evaluation of organic causes of erectile dysfunction is reaching a high level of sophistication. The patient's history however remains the most important aspect of the evaluation. The history provides insight not only into the etiology of the problem but also into the patient's compliance with the various possible therapeutic options. Visual sexual stimulation, intracavernous pharmacostimulation and/or nocturnal penile tumescence testing may confirm the history obtained from the patient. By duplex scanning performed after intracavernous injection of papaverine (or another vasoactive drug) one may uncover an impairment in arterial blood flow. Venous leakage may be demonstrated by dynamic cavernosography.

Recent appreciation of the neuroanatomy and neurophysiology of erection makes it possible to assess neurogenic impotence. Of course, clear cut neurologic deficits such as spinal cord injuries and peroperative damage are quite evident, but others might require more extensive evaluation. Penile biothesiometry, dorsal nerve somatosensory evoked potential tests as well as demonstration of the bulbo-

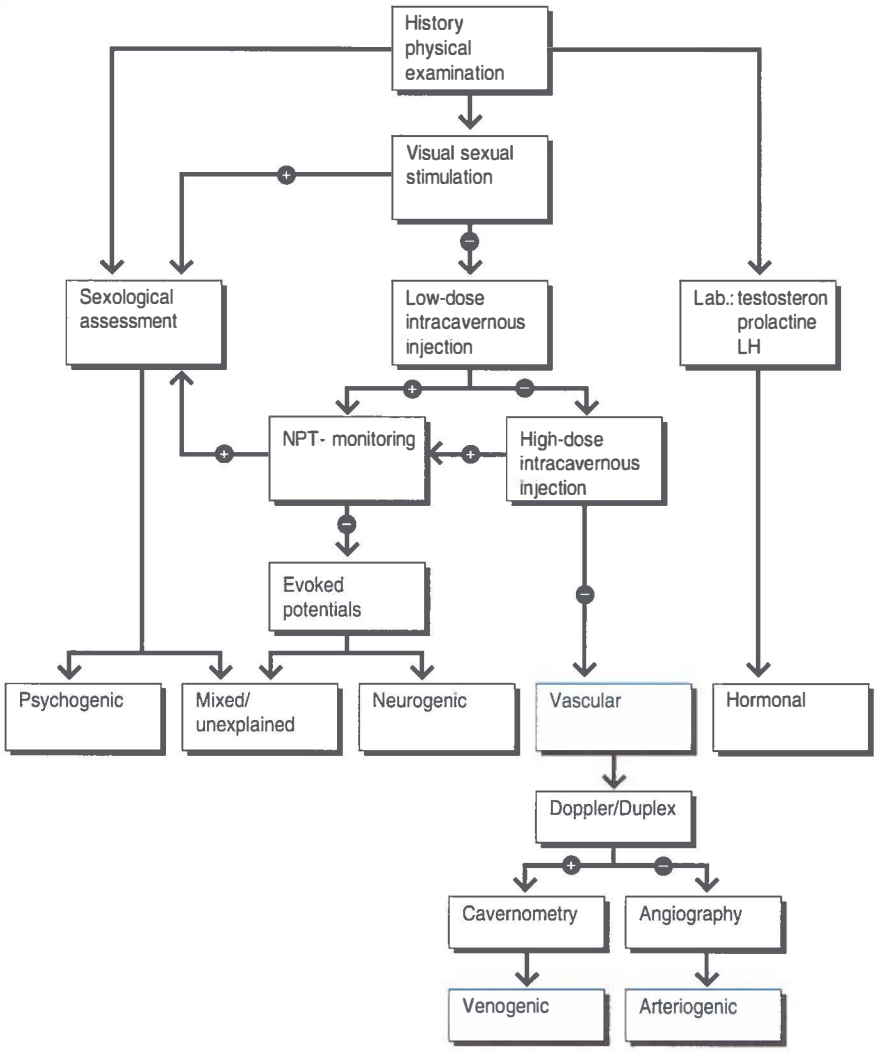

Figure 4 Diagnostic approach advocated by the Dutch Society for Impotence Research (1990).

cavernosus reflex response are all clinically available methods of assessing neurogenic erectile dysfunction. For autonomic function there are as yet no conclusive clinical tests.

Figure 4 shows the diagnostic approach advocated by the Dutch Society for Impotence Research (1990). This scheme will undoubtedly continue to be adapted. At present there is certainly no world-wide consensus in this regard.

The therapeutic arsenal with regard to erectile dysfunction has been changed markedly. One of the new therapies has been intracavernous injection of either papaverine alone or papaverine and phentolamine. Other agents (such as prostaglandin E1) are also being studied for this application.

It should be remembered that the availability of erection prostheses was probably the single most important impetus to the development of 'Erectile Dysfunction' as a subspeciality in urology. Prostheses continue to be improved and modified and most of the newer devices attempt to preserve surgical simplicity while increasing the esthestic properties.

Vascular surgery for the treatment of erectile dysfunction has involved either microsurgical arterial bypass surgery or operations on venous drainage of the penis. Bypass surgery has usually utilized the inferior epigastric artery as a neoarterial source, and an anastomosis between this vessel and the interconnected dorsal artery and dorsal vein of the penis has gained popularity in the last few years. Another option is deep dorsal vein arterialization. Venous surgery is indicated in patients who describe life-long soft erections and show abnormal venous drainage channels on dynamic cavernosography.

In patients in whom the cavernous musculature is intact and who have no significant venous leakage, electrical stimulation may be a successful alternative.[52] Those types of impotencies amenable to this form of treatment include partial arteriogenic impotence and selective cases of neurogenic and diabetic impotence. The hope is that with electrodes implanted on the cavernous nerve, the patient will recover the full ability to initiate and sustain erection by neural stimulation. A few years ago this was just a dream, but recent studies by Tanagho and co-workers indicate that such recovery is attainable, probably in the not-too-distant future.[65]

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CHAPTER 4

MYTHOLOGIC, RELIGIOUS, AND CULTURAL ASPECTS OF IMPOTENCE BEFORE THE PRESENT MODERN ERA

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INTRODUCTION

Since the very first time a penis was found to be soft when it should have been hard, man has known the suffering associated with impotence. A deeply felt sense of inadequacy extending beyond his own sexual satisfaction causes a man to seek treatment for impotence. Frequently he comes to the physician searching for a pill or a magic potion that will painlessly and conveniently cure his devastating problem. Impotence is not only a problem of modern society. Already in old Greek culture the impotent male was considered a sad figure, who was looked upon with more derision than pity (figure 1). Since those early times, centuries ago, man has sought remedies for impotence originally looking much more outside himself rather than within his own mind and body. In this paper we will review and reflect on mythologic, religious, and cultural aspects of impotence before the present modern era, especially before the beginning of the 18th century.

Early cultural impact of potency

In the earlier prae-historical times, when men at first became cultivators of the land, temporal and spiritual power was combined in the person of the priest king. Where the existence was so precarious and dependence upon successful crops so complete, the effect of the well-being of the king upon the success of the harvest was a common belief. Thus the king's health and strength, and his sexual potency in particular, were of vital interest to all his subjects. A king's failure to satisfy any of his numerous consorts sexually was regarded as a fatal sign of decay.[1] The desperation of the individual whose erectile power failed at the right moment is fully understandable, considering the vital importance of procreation for the survival of the group. The most evident proof of good male functioning was to make women pregnant. It took a long time before scientific minds would separate erotic and reproductive functions.

Sexual anxiety in childhood and its psychopathological role in adult male impotence can clearly be recognized in Greek mythology.[2] King Phylacus for instance asked a physician, named Melampus to cure his son Iphiclus of impotence. Melampus then made a sacrifice to the god Apollo whereupon two vultures alighted upon the carcass of the sacrified animal. One vulture then reflected to the other how Iphiclus, as a child, saw his father coming towards him with a blood-stained gelding knife. Terrified by fear that he himself would be gelded he screamed with fright and became impotent. By a process of desensitization to the dried blood and rust upon the gelding knife Melampus was able to cure Iphiclus of his impotence.

In a later period impotence was often considered as a result of a divine curse. In the Histories by Herodotus the story is told of Amasis, King of Egypt, who married

Figure 1 Impotence, Attic disk, 5th age B.C., found in Italy. Münich, private collection

Ladice, a Greek woman. Each time this king went to bed with her he was unable to have intercourse and he resorted to other wives instead. This partner related impotence was believed to be the result of a bewitchment. Ladice, although denying the charge was condemned to death. She then prayed to the goddess Aphrodite asking for consummation of the marriage and her prayers were answered.[3]

Another example from those early times can be found in the Satyricon by Petronius. The author related how Encolpius was punished for his desecration of the rites of Priapus by infliction of impotence. In this condition Encolpius was made to undergo the orgy of Priapus's priestess Quartilla:

"With her hand she began to stroke that part of me which by now was cold as ice and shrivelled with a thousand deaths".[2]

Religion and impotence

In the polytheist Greek-Roman systems a divine entity usually symbolized virility and its portrait figured an erect penis.

In Celtic religion menhirs were erected as signs of virility. These menhirs were also used to find a remedy to impotence as well as to sterility. The druids used to cut mistletoe because its sap looked like sperm. Drinking this sap they made a propitiatory and exorcising ceremony for its participants.[1]

The Chinese approached the problem of impotence more philosophically:

"Strong passions reduce and exhaust the emanations, whereas moderate passion strengthens the emanations and make them fertile. Strong passion consumes its emanations, whereas the emanations feed a moderate flame of lust. Strong passion scatters its emanations, whereas a moderate flame of lust begets life through its emanations".[4]

The ancient Hindus noted that impotence could follow connection with a distasteful woman:

"Cessation of the sexual desire owing to the rising of the bitter thoughts of recollection on the mind of a man, or a forced intercourse with a disagreeable woman (who fails to sufficiently rouse up the sexual desire in the heart of her mate) illustrates an example of mental impotency".[5]

Some of the remedies and their very interesting results are described in the Samhita of Sushruta:

"Powders of sesamum, Másha pulse, Vidári, or S'áli-rice should be mixed with Saindhava salt and pasted with a copious quantity of the expressed juice of the sugar cane. It should then be mixed with hog's lard and cooked with clarified butter. By using this Utkárika a man would be able to visit a hundred women. Bij eating the testes of a he-goat with an adequate quantity of salt and powdered long pepper, fried in clarified butter prepared from churning milk (and not from curd) a man is enabled to visit a hundred women one after the other. Powders of dried malaka successively soaked in its own expressed juice should be licked with honey, sugar and clarified butter, after which a quantity of milk should be taken. This compound would make even an old man of eighty sexually as vigorous as a youth".[6]

The Samhita of Sushruta is one of the best known so-called Vedas. The Ayur Vedas - or Poems of the Science of Life were finally thought to have been inscribed in about 2000–1000 B.C., but by that time had been in existence for many many years.

Other examples of potency problems in ancient literature are Biblical ones. A passage in Genesis describes how Abimelech became impotent as a divine punishment for taking Abraham's wife:

"But God came to Abimelech in a dream by night, and said to him: Behold, thou art but a dead man, for the woman which thou has taken for she is a man's wife".[7]

In the first Book of Kings an attempt to cure a potency problem is described:

> *"Now king David was old and stricken in years; and they covered him with clothes, but he got no heat. Wherefore his servants said unto him, Let there be sought for my lord the king a young virgin: and let her stand before the king, and let her cherish him, and let her lie in thy bossom, that my lord the king may get heat. So they sought for a fair damsel throughout all the coasts of Israel, and found Abishag a Shunammite, and brought her to the king. And the damsel was very fair, and cherished the king, and ministered to him: but (as the old text says) the king knew her not".*[8]

The monotheist religions turned out to have an ambivalent attitude towards potency. The Islamic prudishness did not prevent its believers from praying to Allah before intercourse: a prayer to avoid impotence.[1] In the Middle East for that matter derision towards real or supposed impotent men was more severe than elsewhere. Fearing a failure the Islamic Arabs also consumed big quantities of aphrodisiacs like hash, red pepper and grinded horn. Consequently the rhinoceros in Africa became an endangered species because of the demand for its horn as an aphrodisiac.

Witchcraft and impotence

In the Middle Ages particularly impotence was believed to be due to witchcraft. Impotence produced by sorcery was known as "ligature". According to R.H. Robbins, in his Encyclopaedia of Witchcraft and Demonology, impotence was produced by tying knots in a cord or a strip of leather and then hiding it, and by the administration of potions.[9] The impotence would continue until the cord was discovered and untied; the "ligature" would remain permanent if the cord was not found or if the knots could not be loosened.

The other method involved potions: At the Château de Bassompierre in France an old man married a beautiful young wife but kept his mistress. The wife became jealous and sought advice from a neighbour, who gave her a herb to put in her husband's soup. When the husband woke up the following morning, he found himself impotent. Since he could not hope to conceal it from her for long, he told his wife. Realizing her own loss of connubial pleasures, the wife confessed what she had done, saying that it was all due to the great love she had for him. The lord of the manor was informed; he discovered the witch and forced her to administer another herb to restore potency. The witch was soon afterwards burned to death.

Most demonologists discussed impotence caused by magic. A speciality of German witches would be that they could hide a man's penis in his belly. In Scotland, in 1590, two women were convicted of taking away the privy members from some men and bestowing them on others. Since the intended injury was diabolical, cures were difficult. One recommended coming to friendly terms with the witch.

Thomas Aquinas (1227–1274), the famous Dominican wrote in his Quaestiones Quodlibetales:

> *"The Catholic faith maintains that demons are something and that they can do harm by their operations and impede carnal copulation. They might effect this very simple, for example by causing a man to have an aversion for some particular woman".*[10]

Aquinas also established the distinction between natural "frigiditas", where a man could not sleep with any woman at all, and "ligature" where a man could not have intercourse with just one woman.

A canonic law from about 1140 established four points:

1 Copulation can be prevented by malice.
2 Ligature is allowed only by permission of God.
3 The Devil effects the ligature (curiously enough God allowed the Devil power only over the genitals).
4 Relief may come with God's help by abstinence and prayers.

Trethowan has reviewed the medieval demonological literature on impotence and pointed out the close resemblance between present-day psychodynamic theories on etiology and those put forward by medieval theologians.[11]

Impotence trials

In "Le Tribunal de l'Impuissance" the French historian Pierre Darmon described the persecution of patients suffering from impotence.[12] His study covers the entire period in which canonical (ecclesiastical) law considered it a deadly sin for impotent men to marry, i.e. from the 13th to the end of the 17th century.

The cruel custom of 'impotence trials' is older than the Christian faith but the church has perfected it. Perhaps the church's efforts to stimulate the birth rate had something to do with it as Darmon suspected or perhaps the prelates acted out their fear of castration upon these men. In any case the course of the trials showed that counteracting lust was one of the motives. Patriarch Augustin had dictated that intercourse should always entail the hope of fertilization. Impotent husbands violated the sacrament of marriage like eunuchs and hermaphrodites.

On the other hand, infertility as such was not a reason to annul a marriage for men had to bow to God's will. The sacrament of marriage had been instituted by the Lord in order to prevent unchastity and to regulate propagation of the species. Intercourse was regarded as a good remedy against carnal desires; it was the lesser of two evils. Performing one's 'conjugal duties' was satisfactory even if no children were born as a result. When a husband and wife made love, even though the former was incapable of performing the Official Act, they ran of course by definition a grave risk of violating prohibition of sensual pleasure. And the church had several other rather paradoxical views. Candidate-monks, for example, were carefully and

intimately examined for abnormalities of their genital organs they were forbidden to use. The same morality demanded that marriages between elderly persons, who no longer had sexual desires and lived as brother and sister, should be declared void. Despite all rhetorical praise of spiritual union the Roman Catholic Church (after the 13th century) reduced heterosexual love to its physical consummation.

For a long time 'permanent unsettlement' of a marriage could only be established in cases of bigamy and murder, but after the 16th century more emphasis was placed on impotence because it was more readily demonstrable (!). In this delicate matter the clergy invoked the assistance of physicians.

For lack of effective medical knowledge physicians lost themselves in vague and complex typologies of impotence. They differentiated between relative, respective and incurable impotence and frigidity, impotence due to an accident (not always a valid reason to annul a marriage), impotence resulting from bewitchment, and female impotence (equated with a constricted vagina). Each category had numerous ramifications and exceptions, and dubious cases were debated endlessly.

Lawyers, too, were given a free hand in this uncertain matter, but they defined impotence in terms of fraud rather than as a violation of the sacrament. In the lower classes usually the environment took the initiative for a lawsuit, but in the wealthier classes the wives often acted as plaintiffs. They claimed compensation, much as if they had been sold a second hand car that proved unsatisfactory. Older women made use of the impotence trial to settle longstanding feuds about inheritances and properties. Younger women frequently resorted to this trial to seek revenge for sexual and relational problems.

The frequency of impotence trials increased from the end of the 16th century on. Trial reports were printed and distributed in thousands of copies. The accused were targets of satirical poems and public ridicule. During the trials the sexual functions of the accused were tested in a strictly technical and physiological sense. The victim had to demonstrate his capability of erection and ejaculation. A jury comprised of theologians, physicians and midwives evaluated the performance. The formalistic proceedings of the impotence trials and the pompous rituals surrounding them served also to reaffirm the power of the church. Initially this institute showed still some moderation but in the course of the 16th century the authorities took the leap from spiritual to actual voyeurism. They demanded demonstration of the stiffness of the male organ and its 'elasticity' and 'natural movement' had to be shown. Sometimes a jury even demanded 'proof of an ejaculation'.[12]

In the heyday of the impotence trials even this was no sufficient proof and a defenseless couple had to perform intercourse in presence of a jury. Although everyone complained — you just can't do that — nobody took the first step to end this practice. After all it was "necessary" as a matter of evidence. By decree of the High Court of Paris this church-sponsored 'live show' was abolished in 1677, although in public memory the concept remained alive for many years to follow.[1]

Physical examination — of the male suspects as well as of their wives — was an

important feature of the impotence trials. As such this was not a novelty: even in Roman times a young couple had to submit to examination before marriage. From the end of the 16th century on these genital examinations were subject to discussion. The erection tests were shrugged off, but with regard to the investigation of the 'female shame', prudish indignation was mixed with a hardly concealed excitement. Whatever the female plaintiff did she compromised herself. If she remained married to her impotent husband she shared his guilt in violating the sacrament. If she took action, however, she was suspected of having the kind of knowledge a decent woman should not possess. After annulment of her marriage, the only course open to her was to enter a convent. Then who was more to pity, she or her partner?

There was a temporary setback in these trials when the French Revolution introduced the Code Civil to replace canonical law. But a revival of impotence trials occurred towards the end of the 19th century. Meanwhile marriage had come to be regarded as a civil contract and a husband as well as his wife could request a divorce; but beneath this rational layer, hatred against impotence proved still alive. One may wonder how impotence trials and all these excesses could ever have developed. It seems likely that the 'trial through congress' was instituted by inquisitive physicians and lawyers, who were surprised that a man could be impotent. Their professional blindness was in no way corrected. The church was two-faced, and the bourgeoisie took a lenient view.[13]

The obsessive and very detailed discussions about sexual abnormalities probably served as a verbal outlet to vent the repression of all physical things. The intricacy of complex proceedings and meticulous ecclasiastical 'sexology' inevitably led to this extreme form of administering 'justice'. Every question raised ('Is it legitimate to have intercourse with a woman without ejaculating sperm') led to the next ('Is it legitimate to introduce the penis into any orifice other than the approriate one?') etc.

Physiology of erection, the beginning of science

Among the first ones who considered erectile functioning seriously and in a scientific way were the Italian Leonardo da Vinci (1452–1519), the Frenchman Nicolas Venette (1633–1698) and the Dutchman Reinier de Graaf (1641–1673).

In evaluating Da Vinci's attempt at a functional approach to anatomic problems the urologist Belt quoted Leonardo's remarks on the penis:

> *"The origin of the penis is situated upon the pubic bones so that it can resist its active force on coitus. If this bone did not exist the penis, in meeting resistance, would turn backward and would often enter more into the body of the operator than into the body of the operated"*[14]

For many years erectile power of the penis was considered as the result of pneuma or vital spirit. These theories were abandonned in the Middle Ages and replaced by the belief that air under pressure produced the stiffness of the penis. Leonardo objected to this theory by stating:

"Of the virile member when it is hard, it is thick and long, dense and heavy, and when it is limp, it is thin, short and soft, that is limp and weak. This should not be adjuged due to the addition of flesh or wind but to arterial blood. I (Leonardo) have seen this in the dead who have this member rigid. For many die thus, especially those hanged of whom I have seen an anatomy, having great density and hardness, and these are full of a large quantity of blood, which had made the flesh very red within, and with others, without as well as within. And again, one observes that the rigid penis has a red gland which is a sign of an abundance of blood and when it is not rigid, it has a whitish appaerance."[14]

In France, Venette summarized the general medical opinion when he sadly wrote after mentioning the different methods for treating impotence used at that time:

"If a woman's hand, which is the best of all remedies is not good enough to cure the flabbiness of a man's penis, the other remedies will do little."[15]

Another medical scientist who reported the connection between vascular flow and erection was the Dutch anatomist Reinier de Graaf. He described in 1677 the immediate erection after injection of water into the internal iliac artery in a human cadaver.[16]

Confronted with patients these scientists however were not able to examine impotent men technically, not to classify nor even to cure them.

Conclusive remarks

Nowadays impotence is a medical diagnosis composed of both organic and psychological components. In the past, many forms of male impotence have been attributed to supernatural factors. Although in modern society supernatural impotence seems to be only a marginal agent, it has been found that this cause of impotence still retains an important place in some groups of patients.[17] Therefore it seems worthwhile when one approaches a patient with erectile dysfunction to examine his cultural background and systems of beliefs, and how he conceptualizes and understands his erectile dysfunction, since such an approach can greatly help the therapeutic process.

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CHAPTER 5

PENILE FLOW- AND BLOOD PRESSURE INDEX AND THE EFFECTIVE DOSE OF INTRACAVERNOUS PAPAVERINE

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ABSTRACT

A simple test to predict the outcome of intracavernous papaverine treatment would be helpful in the management of erectile dysfunction.

Doppler studies of the flaccid penis were compared with the results of intracavernous injection of papaverine. There was no correlation between these two variables. Therefore Doppler studies of the flaccid penis are not appropriate to predict the effect of intracavernous injection.

INTRODUCTION

In a large number of impotent men and in normal volunteers erection can be caused by injecting papaverine into a corpus cavernosum. This method has been used for the differential diagnosis and for treatment of neurogenic and vascular impotence.[1]

The first medical scientist who reported the connection between vascular flow and erection was the Dutch anatomist Reinier de Graaf. In the year 1677 he observed immediate erection after injection of water into the internal iliac artery in a human cadaver.[2]

Nowadays less invasive, but sometimes rather complicated techniques to investigate penile circulation are available. These techniques include Doppler auscultation of the penile arteries, penile skin blood flow measurement using photoplethysmography, thermography, radioisotope penography, intra-arterial selective pudendal arteriography and intravenous digital arteriography of the hypogastricopudendal axis.[3]

In our opinion the clinical relevance of these more or less complicated techniques is not yet very well-established.

Before starting patients on autoinjection with papaverine into their corpus cavernosum it would be useful to be able to predict the outcome by performing a simple test. Therefore we studied penile brachial blood pressure (PBI) and penile blood flow index (PFI) by use of Doppler tests in order to try and predict the effect of intracavernous injection of papaverine in the individual patient.

PATIENTS AND METHODS

We studied 18 impotent men, 23 to 69 years old, who had a routine evaluation consisting of a thorough history, physical examination, serum testosterone and prolaction and snap-gauge nocturnal penile tumescence monitoring. The quality of penile circulation was evaluated by calculating the PBI and the PFI.[4,5]

The PBI is the ratio of penile to brachial systolic blood pressure. Penile pressure was measured using a 10 KHz pencil probe Doppler placed over the corpus cavernosum and angled 30° proximally thereby trying to maximize detection of

Table Measurements of PBI, PFI, and the effective dose of papaverine in 18 impotent men

Patient	Age (yrs)	Cause of impotence	PBI (n.0.9)	PFI (n 6.0)	Individual effective dose of papaverine (mg)
1	69	pelvic surgery	0.62	8.1	40
2	55	pelvic surgery	0.62	?	45
3	58	diabetes	0.66	6.6	no effect
4	68	arteriosclerosis	0.66	4.0	80
5	57	arteriosclerosis	0.66	?	100
6	38	pelvic surgery	0.67	2.0	20
7	34	diabetes	0.72	?	no effect
8	48	multiple sclerosis	0.75	3.6	40
9	39	spina cord lesion	0.77	2.9	40
10	31	diabetes	0.77	2.7	no effect
11	62	arteriosclerosis	0.77	6.0	no effect
12	62	spinal cord lesion	0.82	3.1	20
13	39	spinal cord lesion	0.83	3.5	100
14	63	arteriosclerosis	0.90	?	no effect
15	23	venous leak	0.96	2.5	80
16	26	venous leak	0.96	2.7	no effect
17	51	pelvic surgery	?	4.6	50
18	52	pelvic surgery	?	6.8	20

the cavernous artery. PBI of 0.6 or less has been shown to be indicative of vasculogenic arterial impotence while experience with approximately 1000 penile Doppler studies indicate that a normal potent male should have a PBI of greater than 0.9.[6] Therefore we considered a PBI of less than 0.9 but more than 0.6 not specific for vasculogenic arterial impotence.

The PFI measures the average penile artery acceleration (peak velocity/pulse rise time) relative to the radial artery circulation. According to Velcek et al. penile flow indices less than 6 were associated with potency; indices greater than 10 with impotence.[5] Intermediate values contain various degrees of erectile failure and pathology and are also not specific for vasculogenic arterial impotence.

After completion of these tests an intracavernous injection was given.

The dose required for a firm erection of the desired duration – that is, at least 30 minutes but not more than 4 hours – (the effective dose) varies from patient to patient between 20 and 100 mg.

The initial dose was 20 mg of papaverine sulphate. In the case of non-functional response, that is to say an erection lasting less than 30 minutes or the penis being not firm enough for vaginal intromission, the patient was reinjected with increased

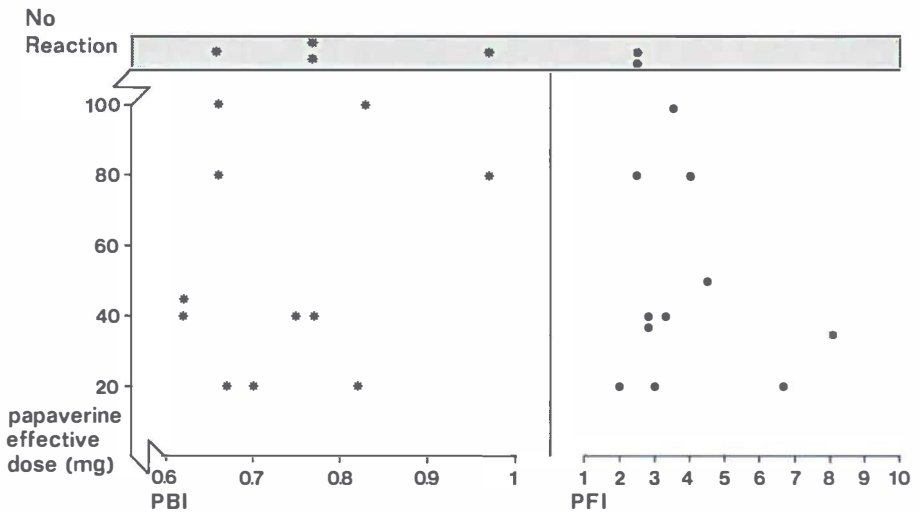

FIG. I Vascular indices and effective doses of papaverine

Figure 1 Vascular indices and effective doses of papaverine

doses of papaverine with increments of 15 mg. This process was continued until a satisfactory erection occurred or until a limit of 100 mg of papaverine was reached. This limit was chosen because papaverine may have a quinidine-like effect on the heart and when directly injected in the circulation in a dose above 100 mg it could cause cardiac arrythmia.[7]

RESULTS

History and physical examination suggested an organic origin of the impotence in all of the 18 patients. The snap-gauge nocturnal tumescence monitoring was negative in all patients nor did the hormonal screening show any abnormality.

Four patients had a known vascular disease, 3 diabetes mellitus, 4 neurologic disease, 5 had undergone major pelvic surgery and 2 had a history suggestive for venous leak impotence (table).

Because of technical problems in 2 patients a PBI could not be identified. A PBI of 0.9 or more was found in 3 out of 16 patients while 13 had an index of less than 0.9 but more than 0.6. Values less than 0.6 were not found.

In 4 patients no PFI could be determined. In no patient a PFI higher than 10, suggesting vascular disease, was found. In 10 patients this index was less than 6.0, in 4 patients we found unspecific values between 6 and 10.

Both the PBI and PFI are plotted against the response to papaverine injection in figure 1. In 12 out of 18 patients erections, lasting at least 30 minutes and firm enough for vaginal intromission, were achieved within the maximal permitted dose of 100 mg. The required doses varied from person to person and ranged between 20 and 100 mg.

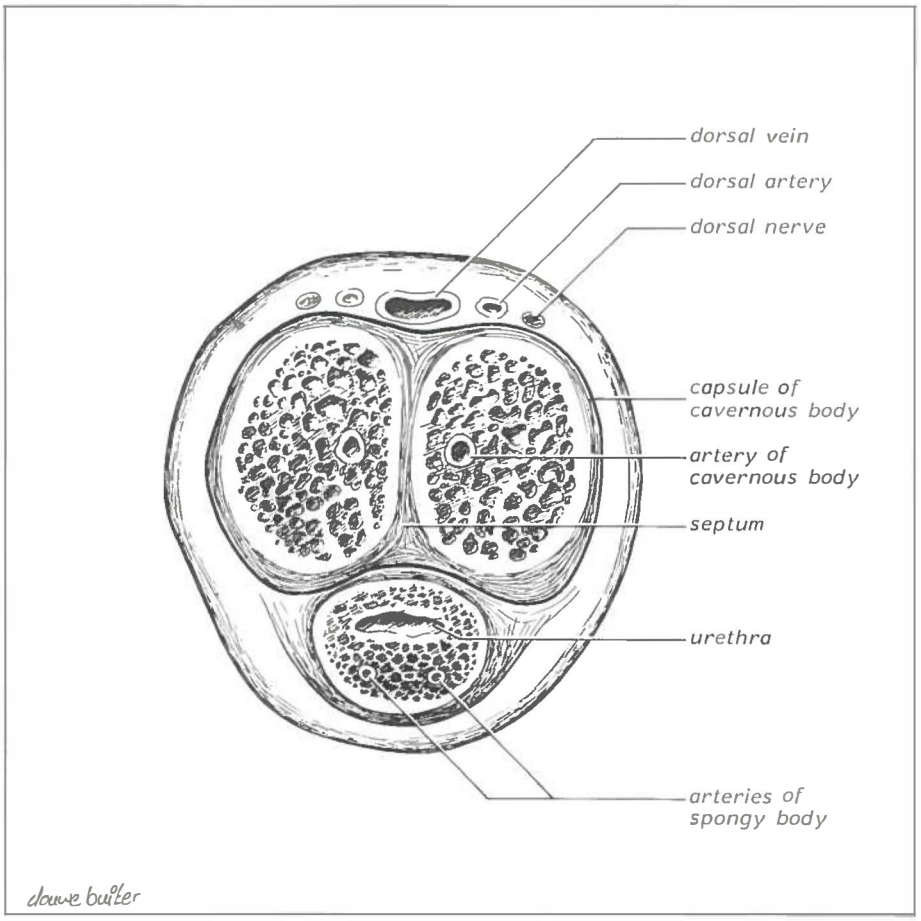

Figure 2 Transverse section through the penis

Of the 13 patients with a PBI lower than 0.9 four did not respond to papaverine injection. In the responding patients no linear relation between the level of the PBI and the effective dose of papaverine was present. In 8 of the 10 patients with a normal PFI an erection was produced by papaverine injection but a correlation between the PFI level and the effective dose was not present (figure 1).

DISCUSSION

This study was designed to investigate whether simple non-invasive Doppler tests could provide information about the effect on erection after intracavernous injection of papaverine in the individual impotent patient.

We found poor correlation between the results of PBI and PFI measurements and the effective dose of papaverine. One of the reasons could be, although tracing of the dorsal artery in the flaccid penis generally is readily obtained, the questionnable validity of tracing the cavernous artery. We suspect pulses presumably from the cavernous artery to be rather from one of the branches of the dorsal artery or the dorsal artery itself, while true cavernous artery pulsations may only be detectable using this technique in an erect penis.

In the flaccid penis most of the arterial blood is carried through the dorsal and spongy body arteries and the flow of blood into the cavernous spaces is very low (figure 2). The observation that rarely more than one drop of blood can be aspirated from a corpus cavernosum in a flaccid penis is illustrative for this explanation.

Lue and his co-workers have demonstrated a better method to evaluate penile vascularization by combination of resolution ultrasonography and pulsed Doppler spectrum analysis of the penis in a flaccid as well as in an erect, papaverine (60 mg) induced, state.[8] This method is supposed to quantify blood flow through all deep and dorsal arteries.

Both diameter and flow velocity in several arteries are measured. If the arteries dilate and demonstrate adequate flow during papaverine induced erection arteriogenic impotence is unlikely. However, if the degree and duration of erection is not normal, venous leakage is possible and the patient should have dynamic cavernosography.

In the management of impotence one should be aware of the psychological inhibition which may influence the results of this kind of investigation including nocturnal penile tumescence monitoring (NPT). However this NPT monitoring should preceed any invasive investigation or planning of vascular or prosthetic surgery.

CONCLUSION

This study confirms the limited value of PBI measurements on the non-erect penis to predict the outcome of intracavernous injection of papaverine.[9]

The same holds for PFI indices.

So the only way to be sure if intracavernous injection of papaverine will work is to try it.

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CHAPTER 6

INTRACAVERNOUS PHARMACOTHERAPY: PSYCHOLOGICAL, SEXOLOGICAL AND MEDICAL ASPECTS

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ABSTRACT

This study assessed psychological, sexological, marital and medical aspects of intracavernous (i.c.) self-injection in the treatment of erectile impotence. Initially seventy-six percent of patients (N=99) achieved a functional erection after injection. In the dosage determination- and training phase a quarter of the responders refused further treatment on grounds of inability to accept this form of treatment or because of varying responses, including recurrence of spontaneous erections. Some patients discontinued because of side effects such as ecchymoses and/or prolonged erection. Self-injection treatment was associated with unchanged libido (59%), low injection frequency (59% once a month, 38% once a week and 3% twice a week), adequate erection rigidity (88%), and improvement (40%) or unchanged (55%) satisfaction with orgasm. The reasons for discontinuation during the treatment phase were loss of sexual interest, partner resistance, loss of adequate responses or persistent problems with regard to self-injection, technically as well as psychologically. Side effects of self-injections included ecchymoses, nodule development and pain. Erection lasting longer than 6 hours occurred 11 times. Persistent fibrosis only occurred in 2 of these patients. Our long-term study demonstrated that one third of the responders do remarkably well. Couples who could not carry on sexual intercourse for several years are now able to do so on a regular basis. The self-injection therapy had also a positive impact upon their marital and psychological well-being.

INTRODUCTION

There is a great pressure in the western society to be sexually attractive and able. Demands on men are heavier than on women. Males are vulnerable concerning erectile potency which may arise out of organic problems but also out of ignorance, cultural inhibitions, unrealistic expectations, and/or performance anxiety. A trained urologist, medically as well as surgically, must be aware of those factors and be able to identify them. An understanding of the psychological aspects of sexuality is a prerequisite even when medical or surgical treatment of impotence is clearly indicated.

During the last six years many urologists have been very active in treating erectile dysfunction with intracavernous self-injection therapy using vasoactive drugs.

Initially concern about its (side-) effects has been focussed upon medical problems such as a prolonged erection or development of fibrosis in the corpus cavernosum.[1,2,3]

Up till 1991 literature about its impact upon sexual, psychological, and marital functioning is however limited.[4,5] Furthermore information about the reasons for discontinuing of this form of therapy by some patients is scarce.[6]

The goal of our study was to obtain more information about 1. the reasons and period of time of discontinuation, 2. the impact of i.c. self-injection therapy upon sexual, psychological and marital functioning and 3. medical complications of intracavernous pharmacotherapy.

PATIENTS AND METHODS

From December 1984 till December 1990, 267 patients with potency complaints were referred to our erectile dysfunction clinic. To determine the etiology they underwent a series of noninvasive screening tests. These tests included history, physical and neurological examinations. Biochemical tests such as determination of serum levels of testosterone, luteinizing hormone, follicle-stimulating hormone and prolactin were performed routinely. Penile blood pressure with calculation of penile brachial index (and in a later phase by duplex scanning of the cavernous arteries) was scored in almost all patients as well as measurement of nocturnal penile tumescence and rigidity using a snap-gauge device (in a later phase an ambulatory rigidity-tumescence monitor was used). In patients with an obvious underlying etiology, such as spinal cord injury, these tests were limited to history and a physical and neurological examination. If the etiology seemed unclear, patients underwent additional tests such as bulbo-cavernosus reflex latency time measurement, cavernosometry and -graphy, selective pudendal angiography and/or psychological screening.

Intracavernous injection therapy was recommended as an option for any patient with organic erectile failure with the exclusion of patients with hypergonadotropic hypogonadism, who received hormonal treatment. Patients with coronary heart disease, liver disease, sickle cell disease or patients on anticoagulant therapy were excluded from this study because of the fear of complications (see Chapter 3). In a patient with psychogenic erectile failure, injection therapy was only considered as an option if he had either failed to benefit from sex therapy, or if he was not an appropriate candidate for sex therapy.

Before any decision towards the injection therapy was made all patients were extensively counseled regarding its effectiveness and possible complications. Ninety-nine patients entered the clinical trial of i.c. self-injection therapy.

Therapeutic protocol

The i.c. self-injection therapy protocol consisted of 3 phases:

I a dosage determination phase, in which a series of increasing doses of the vasoactive agent were injected into the corpus cavernosum and the minimal dose to produce a functional erection was established,

II a training phase in which patients or their partners were taught the technique of self-injection and,

III a follow-up phase, in which patients practiced i.c. self-injection therapy at home, not more than twice a week and with the formerly established optimum drug dose.[7]

The 'vasoactive' drug used was papaverine sulphate to a maximum dose of 100 mgs. By inadequate erection a mixture of papaverinesulphate and phentolamine (30:1)

was used. A dose was considered sufficient if an erection of at least 30 minutes duration with adequate rigidity followed.

Follow-up

All patients were seen for a follow-up examination every 3 months during the first 2 years after the initiation of this therapy. At each follow-up visit they were given enough medication, syringes and needles to last until the next visit. After 2 years the follow-up period was stretched to twice yearly.

At these follow-up visits patients had a physical examination and were asked to rate their overall satisfaction with i.c. injection therapy as satisfied, indifferent or dissatisfied. Injection frequency, drug dosage, duration and rigidity of the erection, orgasmic function and complications were noted. Patients were encouraged to provide any additional information they believed pertinent to their experience with i.c. injections.

For patients who dropped out of the program we recorded their reasons and the phase at which they dropped out. They were asked whether they preferred implantation of an erection prosthesis or the use of a vacuum-assisted erection device or no further therapy at all.

Information obtained from outpatient records and from the patient himself at the follow-up visits were recorded on standardized data collection forms.

Additional detailed information about the past and present sexual functioning was assessed by a separate questionnaire for patients (and their partners) who had continued i.c. self-injection after the training phase.

With regard to sexual functioning the following items were investigated: sexual behaviour and satisfaction, motivation/libido, genital (penile) sensations and sexual capacities such as erections, orgasm and ejaculation. Questions about over-all satisfaction with i.c. injections and about the reason for discontinuation provided information about psychological functioning. Partner's opinion gave information about marital functioning. All data were processed using standard score counts.

RESULTS

From the 267 patients referred with erectile dysfunction 115 fell out of the study because of either psychogenic impotence or contraindications. From the remaining 152 patients 53 declined the therapy proposal because of fear for noncompliance or side-effects. So ninety-nine patients entered the i.c. self-injection therapy trial. Of these 79 (79%) were impotent from organic causes, 14 (14%) from psychogenic causes and in 7 (7%) the etiology was mixed (table I). The mean patient age was 53 years (range 20 to 75).

In seventy-six patients (77%) a functional erection was achieved during the dosage determination phase. A total of 23 patients (23%) did not respond to the maximal dose of 100 mg papaverine intracavernously or to the maximal dose of 30 mg

TABLE I
Etiology of impotence in patients divided in different groups

	entering	non-responding	discontinued in phase I/II + III	active
	N = 99	N = 23	N = 50	N = 26
neurogenic	35	1	7 + 14 = 21	13
diabetes	23	8	3 + 6 = 9	6
arteriogenic	16	8	4 + 4 = 8	-
venogenic	2	2	-	-
endocrine	2	-	1 + 1 = 2	-
psychogenic	14	2	2 + 5 = 7	5
mixed	7	2	1 + 2 = 3	2

papaverine plus 1 mg phentolamine. The etiology of impotence in this subgroup is given in table I. Of these 23 non-responding patients 7 chose implantation of an erection prosthesis, 2 opted for vacuum assisted erections and 14 wanted no further therapy.

Discontinuing Intracavernous Pharmacotherapy

A total of 18 (29%) out of 76 patients who had functional erections discontinued the program early in the dose determination- or training phase for reasons listed in table II. The mean age of this group of 18 patients was 57 years (range 25 to 47). Of these 18 patients only one chose for implantation of an erection prosthesis, and 2 opted for vacuum assisted erections and 15 wanted no further therapy.

A total of 32 of the 58 patients in phase III discontinued treatment after some time. The etiology of impotence in this subgroup is also given in table I. They cited mainly the same reasons as those who discontinued in the earlier phase, except loss of sexual interest (table II). The number who mentioned loss of sexual interest and the number of patients who regained spontaneous erection is remarkable.

The over-all discontinuation rate in our series is 66 percent. The age range of all discontinuing patients was 25 to 75 years with a mean of 56.

Only 26 patients continued the program. The age range of these patients is between 20 to 69 years with a mean of 48. Of these 26 patients 13 have impotence due to neurological diseases. In 6 patients the etiology of impotence is diabetes and in 5 other patients psychological causes attribute to the erectile dysfunction. In 2 patients the etiology is mixed. The mean follow-up of this group is 23 months (range 2 to 80 months).

TABLE II
Reasons for discontinuing vasoactive intracavernous pharmacotherapy

	dosage determination- or training phase (18 patients)	self-injection phase (follow-up) (32 patients)
pain	4	1
self injection	6	9
fear of needles	5	5
nodules/fibrosis	-	2
prolonged erection	4	7
ecchymoses	3	6
variability in response	2	6
inadequate response	5	8
regained spontaneous erections	4	7
artificiality	2	7
partner resistance	3	8
loss of sexual interest	1	9
follow-up inconvenient appointments	1	3
unrelated medical problems	1	6
partner unavailable	1	3
lost to follow-up	-	1
other reasons	2	2
died during follow-up	-	4

(a single patient may mention more than 1 reason)

Psychosexological and Interpersonal Impact of Intracavernous Pharmacotherapy

All patients were encouraged to involve their partner in the decision to start i.c. self-injection therapy. The vast majority (88%) reported positive support from their partners. Three patients (3%) did not inform their partner and 9 (9%) had no partner at the time of decision to start with this therapy.

Six out of the 58 patients continuing i.c. self-injection therapy after the training phase (10%) changed their relationships. Of those patients with the same partner at the time of follow-up as at the beginning of the i.c. self-injection therapy, 50 percent reported that the i.c. self-injections had improved the overall quality of their relationship, while 45 percent reported that their relationship was unchanged, and 5 percent found it worsened because of the self-injection program (figure 1).

Sixteen patients (28%) reported increased libido at the time of follow-up as compared to pretreatment condition. Eight patients (13%) reported decreased desire. No change was reported by 34 patients (59%) (figure 2).

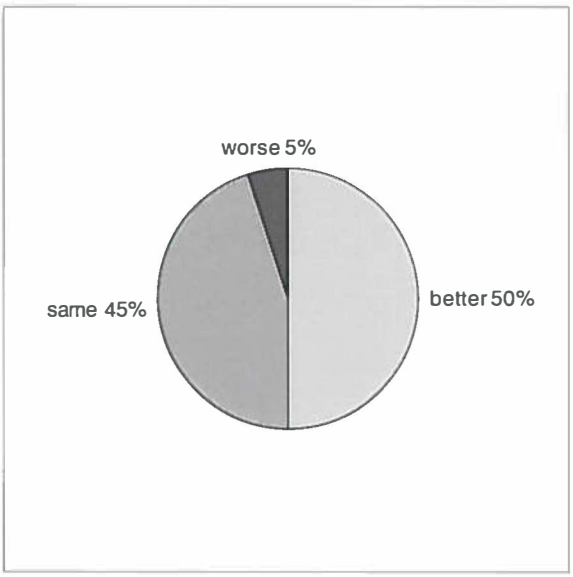

Figure 1 Quality of relationship

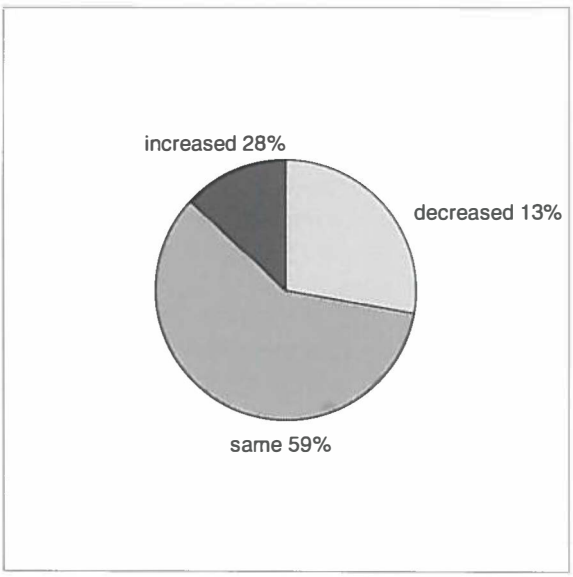

Figure 2 Libido

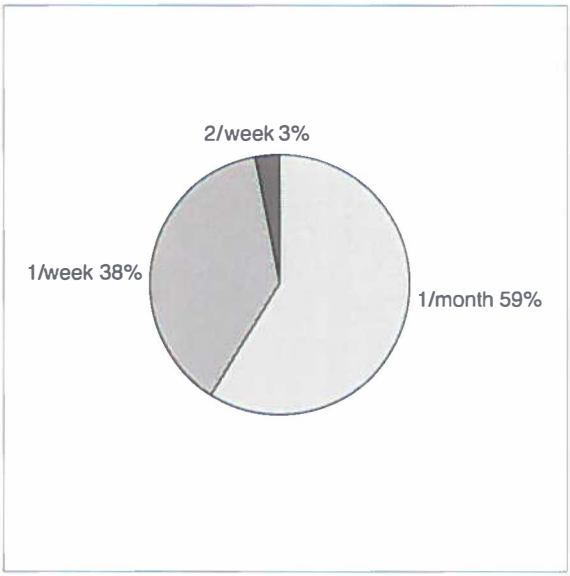

Figure 3 Frequency of intercourse

Thirty-four of the 58 patients (59%) who continued after phase I reported injection induced sexual intercourse once a month. Twenty-two patients (38%) reported to inject themselves once a week and 2 (3%) twice a week (figure 3). The majority (88%) was satisfied in terms of the frequency of intercourse.

Of these 58 patients on self-injection therapy 51 (88%) were satisfied about the rigidity of the papaverine induced erections. Fourty-three percent reported minor variability of response, either in quality of erection or duration. However, only 12 percent experienced erections that were occasionally inadequate for intercourse. In 12 patients (21%) it was necessary to increase the dosage of papaverine and in 7 (12%) the dosage could be reduced. A total of 18 patients (31%) claimed to have return of spontaneous (partial) erections during sexual activity (table II).

A total of 23 men (40%) reported improvement in their satisfaction with orgasm (figure 4). Only 3 patients (5%) believed the quality of orgasm with papaverine induced erections to be less satisfactory.

Partner evaluation

Fourty-three of the 58 questionnaires mailed were returned (74 %), 9 questionnaires could not be evaluated since 3 partners had died and 6 patients had no partner at the time of evaluation. Fifteen partners did not respond to the questionnaire. So sexual and marital function of the partner could be assessed in 34 partners of the 58 men who continued i.c. self-injection therapy after the training phase.

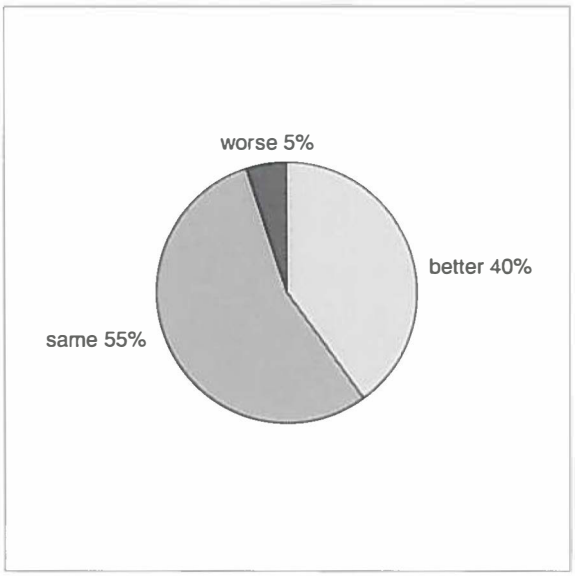

Figure 4 Satisfaction with orgasm

Eighteen out of these 34 partners (52%) were satisfied with the frequency of intercourse. While 8 partners (24%) reported to want intercourse even more frequently. Twenty partners of the patients continuing in phase III (N=26) were also satisfied with the frequency. These partners experienced less difficulties in sexual contact than the partners of the patients who discontinued therapy.

Partner's satisfaction with i.c. therapy was unchanged in 50 percent. Improved performance was reported by 20 percent and 30 percent reported negative results. Both patients and partners were asked whether, knowing the procedure and effects of self-injection, they would have started i.c. therapy again. More than 90 percent of the men said "definitely yes", and 70 percent of the partners were of the same opinion.

Complications of Intracavernous Pharmacotherapy

Medical complications were common (table III). One complication was identified in 18 (31 %) of the 58 patients in phase II and III. In 16 (28%) more than 1 (between 2 to 3) complication was identified. Twenty-four patients (41%) had no complications at all.

Pain during injection was reported by 5 patients (9%). Ecchymoses were noted in 19 patients (33%). Superficial swelling of the penis without ecchymosis occurred in 5 patients (9%), probably caused by subcutaneous injection.

TABLE III
Complications of Intracavernous Pharmacotherapy in 58 Self-injecting Patients

COMPLICATIONS	number of patients
Severe pain	5
Ecchymoses	19
Superficial swelling	5
Urethral injection	4
Injection of desinfectans fluid instead of papaverine!	1
Nodules	7
Persistant fibrosis	2
Erection > 6 hrs	11
Erection > 12 hrs	1
Abnormal liver function test	1

(A single patient may experience more than 1 complication)
(Total no. of injections 2234)

Erection lasting longer than 6 hours was cited by 11 patients (19%), in 4 during the dose determination phase I and in 7 during phase II or III. Only 1 patient experienced erection for more than 12 hours. Except for this last patient all other prolonged erections could succesfully be managed with epinephrine intracavernously (0,01 mg/10ml 0,9% saline). These prolonged erections were limited to patients with neurogenic and psychogenic impotence.

Penile nodules occurred in 7 patients (12%). It could not be ascertained whether the nodules involved the tunica albuginea or the corpus cavernosum. All but one resumed injection therapy successfully after six weeks of abstinence. The total number of injections (2234) was calculated by multiplying the injection frequency with the duration of the self-injection program. There was no significant difference in the total number of injections between men with and without nodules, although men with nodules injected more often than those without. Persistent fibrosis occurred only in 2 patients both after prolonged erections (one of them experiencing an erection of more than 12 hours duration).

DISCUSSION

Sex therapists have criticized the absence of a long term evaluation of intracavernous self-injection therapy with regard to patient satisfaction, the impact on non-sexual adjustment, and the lack of adequate partner evaluations. We were very lucky with the response on the questionnaire in evaluating the patients' partners. Because an impotent man always feels that his masculinity, and not his sexuality,

is threatened[8], appreciation of his expectations with regard to intracavernous self-injection therapy goes beyond needles and syringes into the psychological realm of needs, hopes and wishes. Dealing with such expectations requires time and psychological sophistication on the part of the urologist.

It is realistic to recognize that some men already knew at the moment we offered injection treatment that they could not bring themselves to carry out the i.c. self-injection, but were not able or willing to communicate just that. Also it must be realized that a meticulous listing of potential side effects will frighten some patients, and that verbal attempts to provide some perspective may only be partially effective. Some patients will benefit from adjunctive help from a nurse to gain more comfort and confidence with the idea of injecting themselves.[9]

Furthermore it is important to recognize the disappointment when initial injections (with a low dose out of caution for prolonged erection) fail to produce rigid erections. Perhaps larger initial doses should be given to establish positive expectations.

Our study, along with others, confirms the effectiveness of intracavernous pharmacotherapy in a sizeable percentage of patients.[10,11,12] However, it also indicates that for many patients this form of therapy is not effective and/or unsatisfactory.

Although the 66 percent discontinuation rate in our study is high, high discontinuation rates of 32, 41 and 50% have been reported by others.[10,11,12] Patients who discontinued further therapy (in the dosage determination/training phase and the therapy phase) were from older age group and the majority of them had arteriogenic impotence (table I). These findings may suggest that intracavernous pharmaco-therapy is less effective in the patients who are older or who suffer from arteriogenic impotence.

Of the 32 patients who discontinued during the self-injection phase 24 (75%) reported that the erections were satisfactory for intercourse, which indicates that inadequate response was not the reason for discontinuation.

It is important to stress that a significant difference in the percentages of complications associated with i.c. self-injection therapy as reported in the literature may be related to differences in the methods of follow-up. Some injection programs initiate follow-up only if the patient either reports it personally or sends in the information describing a complication. Maybe patients are reluctant to report complications unless specifically asked at routine follow-up visits. Therefore we believe that routine follow-up visits are mandatory for all patients as long as they remain on injection therapy.

Candidates for i.c. self-injection therapy must demonstrate several specific skills, such as sufficient manual dexterity for syringe handling and visual acuity adequate to find the proper injection site. It is best to instruct both the patient and his partner the injection procedure, even if only the man will perform it. It is much easier for the partner to accept the idea of injections if it is carefully explained to both of them.

As summarized by Zentgraf et al., burning pain in the penis is seldom experienced with the injection of papaverine/phentolamine or papaverine alone.[13] Pros-

taglandine E may cause a long-lasting and very painful sensation during erection.[14]

Other minor side effects, such as ecchymoses (2–10%) and superficial subcutaneous penile swelling are occasionally observed and are caused by improper injection technique rather than by the vasoactive drug itself.[14] Urethral bleeding after injecting into the urethra is rarely seen and always due to incorrect injection technique.

A considerable degree of variation is reported about the incidence of fibrotic changes in the cavernous tissue and tunica albuginea, ranging from 1 to 31 percent.[15,16] These variably sized and shaped areas, described as nodules, plaques or indurations, are presumably due to fibrotic reactions. A distinction must be made between fibrotic lesions inside the corpora cavernosa and changes in the tunica albuginea. The former is probably a reaction of the administered drug itself or its low pH, the latter is more likely due to repeated injections at the same site. The low incidence (12%) of nodules in our patients on self-injection therapy may be explained by the low injection frequency and/or by the repeated instructions. Persistant fibrosis was seen in only 2 out of 58 patients who continued i.c. injection therapy.

During the diagnostic work-up, the overall occurrence rate of priapism (> 6 hrs) is estimated to occur in 3 to 20 percent.[17,18] This complication occurs not frequent due to the fact that the individual dosage for each patient has been determined during the testing period and training phase. Juenemann summarized the published data on long-term results in larger patient groups of 1931 patients who applied 44354 self-injections.[14] Only 160 prolonged erections occurred which shows a probability of only 0.4 percent. The predisposed patient group comprises cases with non-vascular disorders such as psychogenic or neurogenic impotence (as in our series) or who suffer from disorders caused by incorrect injection technique (double injections, higher dosage etc).

Minor variability in response, either in quality of erection or duration, is rather common. This was seen in 25 of the 58 patients in our series, who were or are self-injecting. Explanations include improper technique, drug interference, heavy smoking or psychogenic inhibition.

Levine[11] and Girdley[19] reported the necessity to increase the dosage during the follow-up period in order to achieve a full erection (41 and 35%). In our series this phenomenon was seen in 12 patients (21%).

Systemic complications due to injection of the vasoactive drug(s), such as cardiovascular side-effects are infrequent.[10,20] A drop in systemic blood pressure with the injection of higher doses of papaverine has been observed by various authors.[15,21] We observed this complication in 1 patient during the dosage determination phase. Lue et al. recommend placing a rubber band round the base of the penis, prior to injection, in order to prevent this systemic reaction.[22]

Papaverine is considered to be a hepatotoxic agent. Levine et al. recently reported that in 50 out of 111 impotent men taking part in a self-injection program at least one abnormal liver function test was determined.[11] A more detailed analysis demonstrated that 58 percent of these men had an alcoholic background, and

none of the patients displayed symptoms believed to be related to hepatic illness. This coincides with the results of Zorgniotti and Lefleur, who did not detect any changes in hepatic parameters during a 9-month follow-up of patients on auto-injection therapy.[1] Similar results were established by various other authors.[23,24] None of our patients have so far developed any degree of liver dysfunction. One patient had a temporary rise in OT and PT values, probably due to the use of an antibiotic.

CONCLUSION

The first report on intracavernous injections by Virag in 1982 represents a milestone in the understanding and clinical work-up of impotence.[25] In 1984 we felt these intracavernous self-injections might revolutionize the management of erectile impotence. Now we recognize it is not a panacea. Like many other medical or psychological therapies, this form of treatment is not suitable for everyone. Especially in patients with vasculogenic impotence an adequate erectile response may not be achieved.

The reasons for discontinuing i.c. self-injection therapy among our patients highlight its limitations, which may be the fear of self-injecting, a variable or inadequate response, the artificiality of the procedure, partner resistance and, for some in a later phase, total loss of sexual interest.

Yet, in our series one third of the responders do remarkably well. Couples who could not have intercourse for several years are now able to do so on a regular basis. The therapy has also a positive impact upon their marital and psychological well-being. Nowadays intracavernous self-injection therapy has become an accepted treatment for erectile impotence. However, patients should be made aware of possible complications for prolonged erection and fibrosis and the need for regular follow-up examinations.

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CHAPTER 7

INTRACAVERNOUS SELF-INJECTION OF PAPAVERINE IN THE TREATMENT OF ERECTILE IMPOTENCE AFTER MAJOR PELVIC SURGERY

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ABSTRACT

For several years injection of a vasodilating drug directly into the cavernous bodies of the penis has been used to induce an erection. In 19 of 25 men suffering from organic impotence, erections adequate for intromission could be achieved with papaverine sulfate within the maximum permitted dose of 100 mg. These men were taught to inject themselves. Long-term follow-up, in terms of systemic and local complications, is current under study. Intracavernous self-injection with vasoactive drugs will undoubtedly become the first choice of treatment for impotence of neurogenic causes following major pelvic surgery.

INTRODUCTION

Erectile impotence, the inability to achieve or maintain a penile erection sufficient to accomplish coitus or masturbation satisfactorily, is a well-known complication of major pelvic surgery. The incidence has been reported as 0 to 20% after rectum excision for benign disease, 33% to 100% after abdominoperineal rectum amputation, and 85% after radical cystectomy.[1,2] Until recently the only way to restore some erectile function was by implantation of a penile prosthesis. One of the major problems a patient with a prosthesis faces is the constantly enlarged penis. This situation may at times lead to psychological trauma, especially when the patient has no desire for sexual intercourse even though he seems anatomically prepared.

Since 1982, injection of vasoactive drugs directly into the cavernous bodies of the penis has been known to induce an erection.[3] The concept of intracavernous injection by the impotent male himself or by his partner, popularized by Zorgniotti and Lefleur,[4] may become a useful alternative treatment to overcome the above-mentioned problem. In this article we will discuss the practical aspects of this therapy and report our experience with 25 patients, five of whom had undergone pelvic surgery.

PATIENTS AND METHODS

In the period from January 1985 to June 1986, 25 men suffering from organic erectile impotence were entered into a program of intracavernous-induced erection, In five of these men, impotence was caused by major pelvic surgery (table 1). Each patient was admitted to our hospital and the following studies were made: 1) serum levels of testosterone and thyroid hormone, 2) two nights of nocturnal penile tumescence testing, 3) penile systolic blood pressure measurement, and 4) sacral latency testing, that is, determination of the nerve conduction velocity of the bulbocavernosus reflex arc. These tests were performed to confirm the organic origin of the impotence.

After completion of these investigations, the intracavernous injection was given. The initial dose was 25 mg of papaverine sulfate. When the response was not functional, that is to say an erection lasting less than 1 hour, or the penis was not firm

Table 1
Age, cause, and duration of impotence of five patients in a program of intracavernous-induced erection

Patient	Age (yrs)	Cause of impotence	Duration of impotence at start therapy(mo)
A	59	Radical cystectomy	22
B	52	Abdominoperineal rectum extirpation	34
C	38	Abdominoperineal rectum extirpation	90
D	56	Radical cystectomy	9
E	51	Radical cystectomy	60

enough for vaginal intromission, the patient was reinjected with increased doses with increments of 15 mg. This process was repeated until a satisfactory erection occurred or until a limit of 100 mg of papaverine was reached. After obtaining the functional response dose, the patients were instructed in self-injection technique and discharged. At regular 12-week follow-up visits, the results were evaluated.

TECHNIQUE OF INTRACAVERNOUS INJECTION

In our hospital, papaverine sulfate for injection is available in ampoules containing 100 mg in 2-ml vials. The procedure is to take up the needed volume, starting with a 25-mg dose, into a 2-ml syringe, attach a 16x0.5-mm needle, desinfect the skin, and inject into one of the cavernous bodies at the lateral aspect of the penis at the base (fig.1).

The patient should be taught to identify anatomical landmarks: the glans, the ventrally located urethra, the cavernous bodies and the dorsally located neurovascular bundle (fig.2). It is not necessary to inject on both sides because the cavernous bodies communicate with each other (see chapter 2). The syringe is held perpendicular to the skin at the injection site. Penetration can be felt by a characteristic "give" when the needle passes through the fibrous capsule of the cavernous body (fig. 2). It is not helpful to withdraw blood from the cavernous space into the syringe. Although the success of such an attempt confirms the tip of the needle to be in a vascular space, on the other hand, experience has shown that withdrawing no blood does not prove the contrary (probably because a trabecula may block the tip of the needle in a valve-like manner). The injection time should take 2 to 3 minutes. If this is painful at the start of the injection, one has to stop and reposition the needle correctly before continuing the injection. The patient may feel a tingling

Figure 1 The intracavernous self-injection

sensation in the glans, but there should be no pain. Good visibility and illumination during needle insertion are important to avoid passing through a superficial vein. After the needle has been withdrawn, external pressure by the index finger and thumb is applied for 5 minutes to avoid extravasation of blood from the cavernous body at the puncture site.

After completion of the injection, the penis begins to swell. The full effect is usually reached after 15 minutes. Standing posture of the patient accelerates swelling, probably by decreasing the penile venous outflow. For the next 1 to 2 hours, the penis is firm enough for vaginal intromission.

PRECAUTIONS WITH REGARD TO POTENTIAL COMPLICATIONS

To avoid serious problems, the patient must report back if a rigid erection is still present 6 hours after the injection. During a sustained erection, the blood within the cavernous bodies begins to lose oxygen and accumulates carbon dioxide. The blood viscosity increases and its color becomes darker. Sludging of cellular elements may occur and eventually edema and thrombosis of the vascular channels will result from stasis. Finally, fibrosis of the cavernous bodies can occur, which will lead to a woody and indurated consistency of the penis.

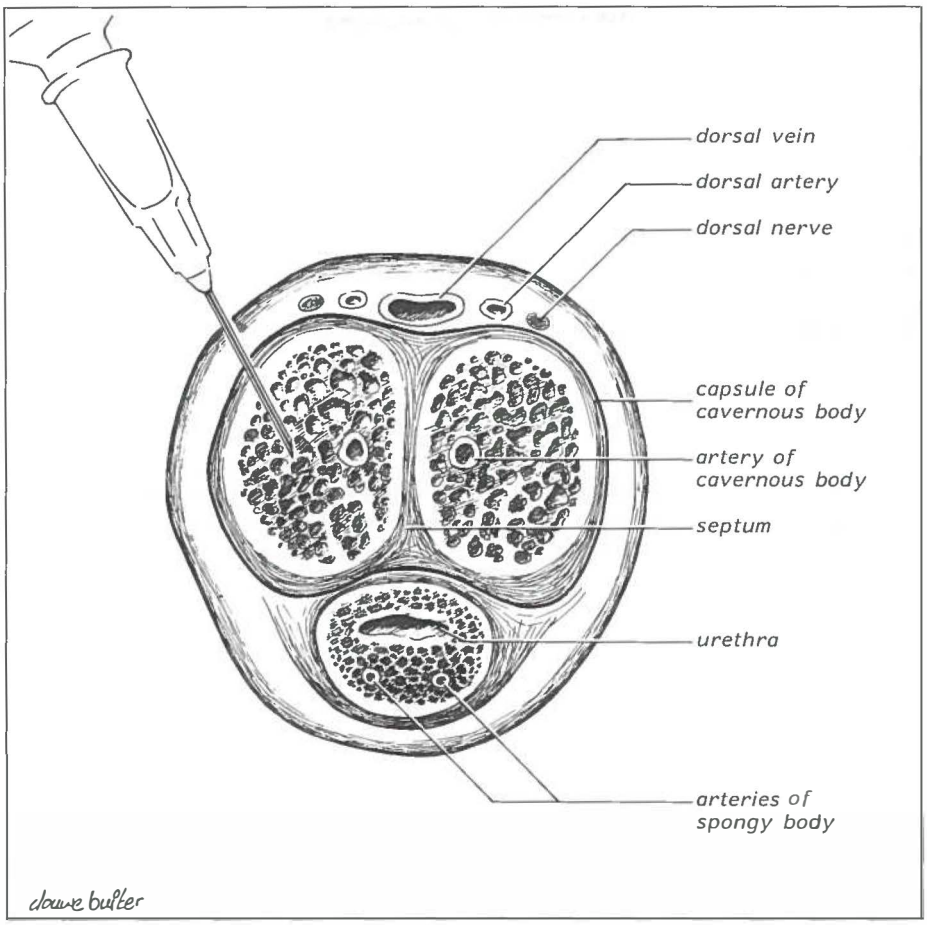

Figure 2 A diagrammatic section through the penis

A sustained erection may be interrupted by a combination of aspiration and intracavernous irrigation with a dilute solution of epinephrine or dopamine.[5] Our procedure is to insert 19-gauge butterfly needles into both corpora, aspirate 5 ml of blood, and slowly inject 5 ml of a dilute solution of epinephrine (0.001 mg/ml) in saline into both cavernous bodies.

Other local complications of the intracavernous self-injection therapy are subcutaneous edema, hematoma, and urethral bleeding. Proper patient instruction, however, may prevent these complications. Potential systemic side effects of papaverine after intravenous administration are facial flushing, dizziness, drowsiness, headache, nausea, elevation of the activities of liver enzymes, and, when given in high doses, cardiac arrhythmias.[6] With the exception of dizziness none of the above-mentioned complications have been reported after intracavernous injection

Table 2
Individual effective dose, injection frequency, and follow-up periods of five patients, impotent after pelvic surgery, practicing intracavernous self-injection therapy with papaverine

Patient	Individual effective dose of papaverine (mg)	Injection frequency	Follow-up (mo)
A	80	4	19
B	25	4	18
C	20	3	18
D	100	1	17
E	100	7	15

of papaverine.[7] Because of these potential systemic side effects and local penile problems, we followed the patients' progress every 12 weeks for up to 20 months. Frequencies of injections were recorded and physical examination and liver function tests were performed.

RESULTS

Erections adequate for intromission could be achieved in 19 out of 25 men within the maximal permitted dose of 100 mg of papaverine. The six patients in whom an erection could not be obtained had vascular abnormalities such as serious atherosclerotic disease or abnormal venous leak from the cavernous bodies.

The dosage required to achieve a functional response varied from person to person and ranged between 20 and 100 mg. All five patients who became impotent after pelvic surgery responded to the intracavernous injection. The individual effective dose, injection frequency, and follow-up periods of these five patients are given in table 2.

In the course of follow-up periods ranging from 2 to 20 months, our patients received a total of more than 800 self-injections. Two patients experienced a sustained erection only twice. In these patients aspiration of intracavernous blood and injection of 5 ml of the dilute solution of epinephrine (0.001 mg/ml) in each cavernous body resulted in a significant detumescence and relief of symptoms. Both patients subsequently responded favorably to a decreased dose of papaverine and currently are still practising the papaverine-induced erection method.

Other complications were a small subcutaneous hematoma (eight incidents) and minor urethral bleeding (two incidents).

Complaints about systemic side effects of papaverine were not encountered, nor were changes in liver enzymes observed.

DISCUSSION

The presence of a physical disease or deficit known to cause impotence does not imply a causal relationship. In other words, major pelvic surgery does not necessarily indicate the organic origin of impotence. Therefore, especially after the introduction of the implantable penile prosthesis in the early 1970s, numerous tests were designed to help discriminate psychogenic from organic impotence more objectively and to categorize the impotent patients into a vasculogenic, a neurogenic, or an endocrinologic etiologic group. Usually, these tests are performed in a multidisciplinary impotence clinic.

Although many aspects of the physiology of erection remain obscure, certain features are clear. A normal erection is created by an increase in blood flow to the penis and, in addition, redirection of this blood flow to the cavernous spaces. This occurs in response to either psychic or tactile stimuli, or both. The blood supply to the penis comes entirely from the internal pudendal artery, which is a branch of the hypogastric artery. The nerve supplies involved are the nervi erigentes of the parasympathetic plexus, which originate from fibers of the second, third, and fourth sacral nerves. These join with the inferior hypogastric nerves from the sympathetic system and form the pelvic plexus. The latter is located between the rectum and posterolateral part of the bladder. The nervi erigentes innervate and cause dilatation of the pudendal artery and its branches to the cavernous bodies.[8]

By an abdominoperineal procedure for rectal cancer, the parasympathetic fibers of the pelvic plexus are totally destroyed. In the course of a proctectomy for benign inflammatory bowel disease, it should be possible to avoid such damage by dissection very close to the rectum. The erectile failure after radical cystectomy is also of neurogenic origin, although vasculogenic impairment may play a role, especially if the hypogastric arteries have been ligated.

Neurogenic impotence after major pelvic surgery is an important factor, but there are a number of other factors that may interfere with sexual function.

The emotional impact of a stoma may have a deleterious effect upon the libido and upon sexual activity. Practical problems, such as accidental leaking of urine or faeces, too much friction during intercourse, and the necessity to empty the stoma pouch before sexual activity, need to be discussed with the ET nurse. It should be stressed that not all erectile impotence requires therapy. Elderly patients who have satisfactory sexual relationships may often find alternative methods of expressing and enjoying intimacy. However, implantation of a penile prosthesis or intracavernous self-injection therapy should be offered to a patient whose erectile failure is clearly organic and who, along with his partner, is interested in restoring erectile function.

Basically, there are two kinds of prostheses, the inflatable and the fixed. Modifications of the fixed variety include malleable ones that can be bent to position the penis more normally when intercourse is not desired. The inflatable prosthesis, originally a by-product of the development of an artificial urinary sphincter, has the advantage of allowing the patient to start and terminate an erection when desired. However, it is a mechanical device that will fail occasionally and may require

repeated operative interventions. For these reasons some patients reject the possibility of a prosthesis. To these patients a trial of intracavernous papaverine-induced erection can be proposed. At this time there is no way to predict the response of papaverine in an individual patient. A poor response to a 100-mg dose strongly suggests a vasculogenic cause of the impotence. To achieve an adequate erection in impotence of vasculogenic origin, injection of a mixture of papaverine and phentolamine may sometimes be helpful, but many of these patients will be content with a prosthesis. Reconstructive vascular surgery in patients in the younger age group has been advised and encouraging results reported.[9]

Considering the potential complications of intracavernous papaverine self-injection therapy, we advise cautious use for a patient with disturbed liver function tests, cardiac arrhythmia, psychiatric disease, sickle cell anaemia or a history of priapism.

It should be emphasized that the long-term effects of frequent penile injections are yet to be determined. However, one of our patients has injected himself more than 200 times in a period of 20 months and is still capable of full erection and has a complete normal penis. If long-term evaluation continues to show only relatively minor complications, the intracavernous papaverine-induced erection will undoubtedly become the first choice of treatment modalities for erectile impotence after major pelvic surgery. This therapy should be initiated and followed by a urologist who is interested in and equipped for detection and management of possible complications.

Acknowledgements

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CHAPTER 8

ERECTILE DYSFUNCTION IN PATIENTS WITH PEYRONIE'S DISEASE AND CONGENITAL PENILE CURVATURE

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ABSTRACT

A bent penis may be accompanied by pain during erection and intromission problems leading to impotence and also pain felt by the partner. The cause is usually congenital or Peyronie's disease. Multiple and different therapeutic modalities have been advocated with various results. There is no agreement about therapy nor about the first choice. We studied treatment comparing it with natural history. Fourty-four patients with a penile curvature were analyzed. The subjective symptoms were scored using a check list, objective symptoms were photographically documented. Patients were seen at 3 months intervals until a steady state was reached. When pain persisted longer than a year a Nesbitt operation followed. It appeared that patients spontaneously showed a decline of their symptoms after 6–12 months. Twenty-three patients were just followed and 21 had an operation. All surgically treated patients were satisfied with regard to the functional and cosmetic aspects, however, a complete straight penis was not accomplished in four patients. Since fifty percent of the patients showed a decline of symptoms we advocate no immediate treatment. When pain and/or dysfunction persist the Nesbitt operation is a safe and successful treatment.

INTRODUCTION

The name of Francois Gigot de la Peyronie, surgeon to king Louis XV of France, has become synonymous with this rather enigmatic though not uncommon condition (figure 1), although he was not the first to describe it. His report was published in 1743 bearing the title "On some obstacles opposing the natural ejaculation of semen".[1] He reported a fibrous thickening in the shaft, described as "rosary beads" causing pain and curvature with erection in three cases. Peyronie thought the disorder was often associated with syphilis or gonorrhea, and that treatment of the nodules before eradicating the "virus vénérien", for which he used mercury, was useless. To treat the fibrosis, Peyronie advised his patient to bath in the Barege Spa in the Pyrenees mountains. He reported good results with this therapy. Sexual habits must have interested Peyronie, since he noted that the disease was more frequent in "men who give themselves up to the vivacity of their temperament".

Although the clinical features are well recognized, the aetiology of Peyronie's disease is still obscure. The lesion is supposed to begin as an inflammatory process in the areolar connective tissue between the tunica albuginea and the corpus cavernosum.[2] Identical inflammatory processes have been reported also after long-term intracavernous self-injection with papaverine-hydrochloride and phentolaminemesylate.[3] The inflammatory process is mainly perivascular, the earlier lesions appear as a lymphocytic and plasmocytic infiltrate.[2]

Different therapeutic modalities have been advocated such as steroids, vitamin E, potassiumparaaminobenzoate, procarbazine, parathyroid hormone, ultrasound, radiotherapy and surgery.[4] All authors have claimed success and all methods have their detractors.

It is common medical knowledge that whenever a variety of treatments is recommended for a disease, none is specific, and that the aim of treatment is merely

Figure 1 Curvature in Peyronie's disease

Table 1
Primary symptoms of congenital curvature and Peyronie's disease

	Peyronie	Cong. curvature
Pain	20 (61%)	1 (9%)
Impotence	1 (3%)	2 (16%)
Intromission problems	17 (54%)	5 (42%)
Pain felt by partner	8 (25%)	5 (42%)

symptomatic relief awaiting for nature to bring about cessation of the progression, if not regression.[5] This statement has been substantiated by several authors who studied the natural history of Peyronie's disease and concluded that the disease is fully manifest when first seen and that the natural history follows a course of gradual improvement.[6] However, the natural history of the disease cannot be predicted in an individual patient at the time of presentation. Although the pain usually subsides spontaneously within a few months after onset, the outcome with regard to the plaque (and hence the degree of curvature with erection) and the outcome with regard to sexual function is much less certain. Pain or severe curvature can make coitus difficult or even impossible. In addition, observation by the patient of his penile deformity may result in performance anxiety and reduced libido. The same type of problems arises in patients with a congenital penile curvature due to unilateral hypoplasia of a corpus cavernosum. This anomaly is a variation on the theme of hypospadia of the urethra and its surrounding corpus spongiosum, except that it is one of the corpora cavernosa which fail to grow rather than the corpus spongiosum.

Since erectile dysfunction and sexual functioning in both patient groups are important criteria for the patient's evaluation of treatment outcome, and data on this are scarce, we decided to perform an explorative study on pain during erection, intromission difficulties, pain felt by the partner and erectile impotence. In a view of the fact that there is not much advantage of the divers treatment modalities compared with the natural course, we wondered if a conservative attitude is the best initial approach, and under which conditions the urologic knife is allowed to perform its delicate incisions.

We evaluated erectile dysfunction and sexual functioning in both diseases and report our experience.

PATIENTS AND METHODS

Fourty four patients with a penile curvature were examined. In 12 of them it was congenital and in 32 patients it was due to Peyronie's disease. The mean age of

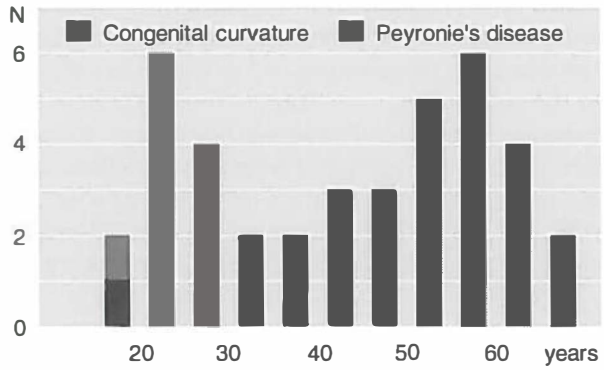

Figure 2 Age distribution at diagnosis (■ Peyronie's disease ▩ congenital curvature)

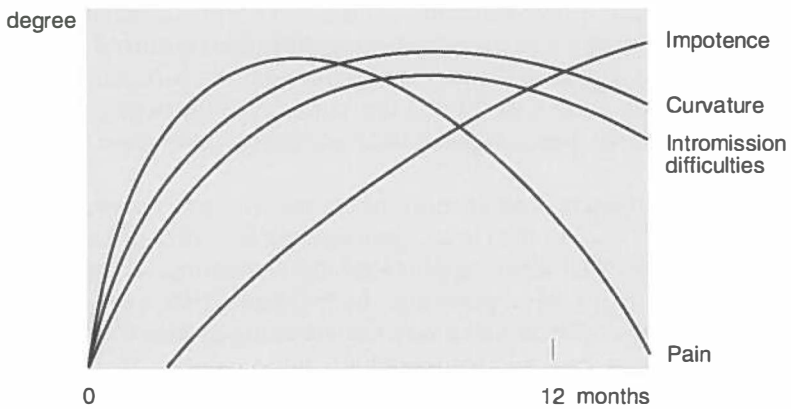

Figure 3 Natural history in Peyronie's disease

patients with Peyronie's disease was 54 years. The primary complaints can be summarized as follows: pain during erection, intromission difficulties, pain during intercourse felt by the partner and the presence of an induration or plaque at the penis (table I). The average time interval between initial complaints and presentation at the clinic was eleven months. Patients with a congenital curvature seek medical advice around the second decade, while patients with Peyronie's disease are usually seen in their fifth or sixth decade (figure 2).

Patients presenting from January 1984 till January 1990 were studied retrospectively. At their first visit a medical history was taken followed by physical examination. Patients were asked to make polaroid photographs of the penis in erection to assess the degree of curvature objectively. Subjective symptoms, such as pain during erection or intercourse, intromission difficulties, pain felt by their partner and erectile impotence were registrated using a check-list. The localisation and size of the

plaque were checked at subsequent visits. If possible, partners were questionned about the frequency of intercourse and sensations of pain during intercourse. By considering this information, the objective and subjective symptoms and the extent of the discomfort was determined and a form of therapy selected.

Initially the treatment consisted of "wait and see policy". Patients were fully informed about their disease and reassured with regard to their complaints. When the complaints persisted or increased during the following year, a surgical correction according to Nesbitt was advised.[7] Patients were seen at 3-month intervals until a steady state was reached, after which they had a final check a year later.

RESULTS

Pain is an important reason to seek medical advice. More than half of our patients with Peyronie's disease complained about pain during erection. This complaint was noted as serious if it prohibited intercourse. Men with a congenital curvature scarcely felt pain during erection. Intromission difficulties occurred about equally in both groups. The degree of the penile curvature did not correlate with the existence of intromission difficulties. More than a quarter of the partners experienced pain during intercourse. This complaint did not correspond with the degree of curvature either.

Complaints of impotence occur more often and in a more serious way in the course of Peyronie's disease than in congenital curvature. Two men with a congenital curvature complained about their sexual dysfunctioning. The main problem was acceptance of their curved penis and the belief that they were insufficient as a sexual partner. One of them had a very traumatic experience when his first sexual partner refused intercourse because of his penile curvature. He could not cope with this experience.

About half of our patients were treated surgicallly. They all had persistence or worsening of their complaints extending over one year. After this period spontaneous regression was not expected. The decision to perform surgery was taken by physician and patient. Without exception the surgically treated patients were all satisfied with the outcome. Complications like infections or neurovascular lesions were not observed.

DISCUSSION

Two predictions can be made about the natural history of Peyronie's disease : The progression of the disorder stops after a while, and in course of time symptoms will diminish (figure 2) or vanish. The curvature will reach a certain maximum deviation and will remain so or decline. Pain is usually the first symptom to diminish. In general, intromission difficulties also decline in course of time; habituation and vanishing of pain are probably of major account.

Erectile impotence, if it occurs at all, is a late symptom. It continues longer and deteriorates while other symptoms decline. The incidence of erectile impotence as a presenting complaint in patients with Peyronie's disease has been reported to be 4 to 5 percent.[8] In our series only 1 out of 32 patients presented himself with erectile impotence.

In a more recent study of 62 hospitalized patients with Peyronie's disease, 30 percent had abnormal noctural penile tumescence (NPT) studies which were in accordance with organic impotence.[9] However, the majority of these patients had an underlying disease or factor other than plaque to explain the abnormal NPT.

For optimal results with surgical correction of the curvature, considering the natural course, the complaints should have been present for at least a year and stable for at least 3 months.

The patient with Peyronie's disease and impotence before operation needs a thorough evaluation of all possible causes. He should have NPT monitoring, a glucose tolerance test, review of all medications and base-line endocrine tests (LH, FSH, testosterone and prolactine) to exclude hypogonadism and hyperprolactinaemia. If these are normal he should have vascular studies. Concomitantly the patient and his partner may need formal psychosexual counseling by a qualified sex therapist for performance anxiety and other relational problems. Patients with organic impotence and Peyronie's disease may require an internal penile prosthesis either at the time of surgical correction of the curvature or as a secondary procedure at a later date.

Congenital curvature of the penis is not in itself an indication for surgical correction. The main problem seems to be that these rather young patients often perceive the deformity as a threat to their manhood. They need a frank and clear discussion about their problem and reassurance that a surgical procedure will be performed if necessary in the future. If the penile curvature causes performance anxiety, referring to the sextherapist may cure this problem.

Photography of the erect penis is an objective method to evaluate the degree of curvature. This can easily be done by the patient himself or by his partner in the privacy of their home or by the urologist after the induction of an erection with intracavernous papaverine injection.[10]

If impotence is defined as the inability to complete sexual intercourse to the mutual satisfaction of both partners then certainly Peyronie's disease and congenital penile curvature are serious disorders which may result in erectile dysfunction and impotence. This impotence, however, can be caused by a variety of disorders, so treatment must be tailored to the individual problem. A conservative attitude initially seems rational.

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CHAPTER 9

TREATMENT OF PRIAPISM BY INJECTION OF ADRENALINE INTO THE CORPORA CAVERNOSA PENIS

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ABSTRACT

Intracavernous papaverine injection has gained widespread acceptance in the treatment of erectile impotence. The opposite problem -priapism- can be treated with the same technique using a vasoconstrictive drug such as adrenaline. We report on eight patients successfully treated for priapism by intracavernous injection of adrenaline.

INTRODUCTION

In Greek mythology Priapus was the god of horticulture, viniculture, apiculture and stock farming, and in general the god of fertility. His image was characterised by an enormous phallus.[5] Priapus lent his name to denote a medical condition -priapism- characterised by a persistent erection that is accompanied by pain and tenderness and fails to subside, even after climax.

Recently, increased appreciation of the pharmacology and hemodynamics of erection, and the introduction of intracavernous injections, have compelled a broadening of this definition to persistence of erection for more than four to six hours. It is a change in pH and oxygenation after four to six hours that initiates the pathologic changes in the corpora cavernosa. An injection-induced erection lasting longer than four hours is called a prolonged erection.

A wide range of surgical and medical treatments has been attempted for priapism, including proximal ligation of the internal pudendal artery, anastomosis of the corpus to the saphenous vein, cavernous spongiosum shunt, cavernous dorsal vein shunt, incision and irrigation of the corpora cavernosa, percutaneous aspiration, division of the pudendal nerves and ischiocavernous muscles, amputation of the penis if associated with malignant disease of the genitalia and so forth.[6]

Medical treatments include deep x-ray therapy, enzymatic lysis of thrombosed blood in the corpora cavernosa, ice packs, sedation, local or systemic anticoagulant irrigation, ketamine, terbutaline, physostigmine, steroids, female hormones, use of hypotensive agents to reduce blood pressure, general and spinal anaesthesia, curare, application of a pneumatic cuff around the penis and more recently intracavernous injection of sympathicomimetic drugs (metaraminol, dopamine, phenylephrine, noradrenaline and adrenaline).[3,4,7,8]

Until recently, our treatment of priapism consisted of surgical establishment of a shunt between corpus cavernosum and corpus spongiosum, or between corpus cavernosum and long saphenous vein. Such a procedure requires general or spinal anaesthesia. Moreover it entails the risk of venous leak impotence. For this reason we chose to treat priapism by percutaneous aspiration and local adrenaline medication in analogy with intracavernous papaverine injection used in the treatment of erectile impotence.

Table 1

Patients treated for priapism

case	age	etiology	duration (hrs)	initial cavernous blood gas values				succesful adrenaline treatment regime
				pH	pCO_2 (kPa)	pO_2 (kPa)	O_2 sat. %	(0.01 mg/10ml saline)
A	64	leukaemia	12	6,61	17,3	0,4	12	+
B	40	ideopathic	6	7,04	12,3	3,3	26	+
C	67	intracavernous injection	8	7,21	6,1	2,1	23	+
D	76	ideopathic	12	6,71	17,6	0,4	1	–
E	59	intracavernous injection	6	7,18	7,2	2,1	21	+
F	58	intracavernous injection	48	6,69	17,3	0,5	1	–
G	66	intracavernous injection	6	–	–	–	–	+
H	51	intracavernous injection	8	–	–	–	–	+

PATIENTS AND METHODS

Eight patients with priapism were treated between January 1987 and December 1989. In five of them, priapism had developed following intracavernous self-injection of papaverine, in one it was the first symptom of leukaemia, and in two patients the cause remained obscure (table 1).

In all cases blood samples were routinely taken for haematological and chemical tests. Both corpora cavernosa were punctured dorsolaterally with a number 21 needle, whereupon in six patients a blood sample was obtained for determination of the pH and the blood gas values in order to establish the severity of the priapism and the degree of ischemia. Next dark blood (sometimes syrupy) was aspirated until bright red blood appeared. When no or insufficient detumescence occurred, 0.01 mg adrenaline diluted in 10 ml of an 0.9% NaCl solution was slowly injected intracavernously, monitoring pulse rate and blood pressure. Before the needles were removed from the corpora, pH value and blood gas values were checked again. Follow up consisted of inspection for side-effects and subjective evaluation of erectile function.

CASE HISTORIES

Patient A, aged 64, was referred to us with an extremely painful erection which had persisted for 12 hours. Two weeks previously he woke up at night with the

same problem; on that occasion the erection disappeared spontaneously after a few hours. Shortly before this he consulted his family doctor for non-specific fatiguability, which remained unexplained. He had previously had a cerebrovascular accident with few remaining symptoms. The patient incidentally used indomethacine suppositories to alleviate back-pain. General physical examination yielded non-specific findings, but both corpora cavernosa were tense. The glans penis (the terminal part of the corpus spongiosum) was found to be pliable. The urinary bladder was empty and rectal examination revealed no abnormality. Blood aspirated from the corpus cavernosum was extremely dark and syrupy. Values were: pH 6.61; pCO_2 17.3 kPa; pO_2 0.4 kPa; HCO_3 concentration 12 mmol/l and O_2 saturation 12% consistent with severe acidosis and ischaemia.

No detumescence ensued after drainage of 300 ml blood, although the colour of blood changed into bright red. Adrenaline injection (0.01 mg in 10 ml 0.9% NaCl solution) primarily also failed to lead to detumescence. The haematological findings meanwhile obtained included a leucocyte count of 244 x 10^9/l. Partly in view of this, another 300 ml blood was drained from the penis, whereupon adrenaline was injected again. This finally led to detumescence. The intracavernous blood gas values had also returned to normal. The consulting physician diagnosed myeloid leukaemia, after which the patient was successfully treated with hydroxyurea. Priapism did not recur and a few months later the patient experienced normal erections.

Patient B, aged 40, was referred to us with a 3-year history of a regularly occurring involuntary erection which initially persisted 1–2 hours but shortly before his visit to the out-patient clinic it lasted 6 hours and became painful. There was no sexual arousal prior to or during these erections. Neither physical activity nor coitus and/or ejaculation did lead to detumescence. Normal erections occurred in between. The further medical history and physical findings were non-specific. Blood morphology, blood chemistry, coagulation tests and hormone profile were all normal.

During subsequent clinical observation priapism occurred in the early morning. Blood gas analysis of the intracavernous blood after 6 hours yielded the following values: pH 7.04; pCO_2 12.3 kPa; pO_2 3.3 kPa; HCO_3 concentration 32 mmol/l and O_2 saturation 26%, consistent with acidosis and ischemia.

Aspiration of 150 ml blood and injection of the adrenaline solution (0.01 mg in 10 ml 0.9% NaCl solution) immediately caused detumescence. The next day a cavernosogram was made to trace possible outflow obstruction due to metastases or thrombosis. Abnormalities were not observed.

After informing the patient about possible complications of surgical therapy and in close consultation with his family doctor, he chose to perform his own punctures, drainage and injections. After instruction this proved a form of simple self treatment. He meanwhile has performed this procedure more than twenty times and has retained his sexual potency.

Patient C, aged 67, called us because of an erection of more than 8 hours duration following intracavernous self-injection of 80 mg papaverine. He had been doing this regularly for two years to cope with erectile impotence following a radical cystoprostatectomy. Pain was not the most prominent symptom. Bloodgas analysis of the intracavernous blood gave the following results: pH 7.21; pCO_2 6.1 kPa; pO_2 2.1 kPa; HCO_3 concentration 18 mmol/l and O_2 saturation 23%, mild acidosis and rather severe ischemia. Intracavernous adrenaline injection (0.01 mg in 10 ml 0.9% NaCl solution) immediately caused detumescence. A few weeks later, a 45-minute erection was induced by intracavernous injection of a lower dose of papaverine (50 mg).

RESULTS

Sufficient detumescence with aspiration alone did not occur. In six cases the priapism was successfully controlled after drainage followed by injection of the adrenaline solution. In these cases the blood gas values returned to normal. One of them developed a small subcutaneous haematoma at the puncture site. No other complications were observed. Their erectile potency turned out to be preserved. Two patients failed the adrenaline treatment regimen: one participated in a papaverine erection programme and had persistent erection for more than two days. The other one had idiopathic priapism 12 hours' duration. In both severe ischaemia and severe acidosis of the cavernous blood was found.

In all eight patients pulse rate and blood pressure remained unchanged during the adrenaline injection procedure and the treatment was tolerated very well.

DISCUSSION

The short-term efficacy of adrenaline injection was apparent in six out of eight cases. Even patient A, who had a serious acidotic and severe ischaemic priapism, was treated successfully. A recent survey shows that five different sympathicomimetic drugs have been used in the past few years to treat priapism.[3] The agent of choice has yet to be identified. In actual practice, adrenaline is freely available but its potential disadvantage is that it has both *a*-adrenergic and *B*-adrenergic actions. If it enters the systemic circulation the *B*-adrenergic effect may cause a marked increase in pulse rate and extrasystoles may occur. This is why a purely a-adrenergic sympathicomimetic drug such as phenylephrine is to be preferred on theoretical grounds.[8]

Others advocate the use of adrenaline simply because of the *B*-adrenergic properties, because *B*-activity may have some added benefit by its action on the venous walls promoting outflow.[4]

Electron-microscopic studies have shown unequivocally that ischaemic priapism in particular requires immediate treatment.[1] Otherwise endothelial lesions will occur after 12 hours, and a few hours later scattered necrotic smooth muscle cells may

be seen in the trabecular network of the corpora cavernosa. After 24–48 hours the endothelium shows very severe damage, and diffuse necrosis develops. Multiple thrombi and damaged nerve endings are also found. After a few days to weeks, the corpora become fibrotic and irreversible erectile impotence results.[2]

An indication for surgery is present when drainage followed by medication fails to induce detumescence. The least complex operation is the Winter procedure, in which a large biopsy needle is used to establish a shunt between glans penis and corpora cavernosa.[9] Then drainage follows through the corpus spongiosum of the urethra and the superficial penile veins, because in priapism the corpus spongiosum is in general not involved. Possible complications of this operation are a lesion of the urethra, infection, necrosis of the glans penis and permanent impotence.

In our opinion initial treatment of priapism by intracavernous injection of a sympathicomimetic drug is preferable to primary establishment of a shunt. In those with severe acidosis and ischaemia of the cavernous blood a shunt procedure may still be necessary, as in our two patients with the lowest cavernous blood O_2 saturation.

In ancient Greece Priapus was among other things the god of apiculture. It is rather striking that today the phenomenon of Priapus can be controlled with the aid of a "sting".

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CHAPTER 10

SUMMARY

In this thesis the findings and results are reported of clinical studies on diagnosis and treatment of erectile dysfunction. In urological terms erectile dysfunction comprises:

- erectile impotence, the inability to initiate and/or sustain an erection.
- a deformed penis (in erection) due to Peyronie's disease or congenital malformities.
- priapism, a persistent erection that is accompanied by pain and tenderness, which fails to subside, even after climax.

The objectives of these studies are described in chapter 1. We had special interest in the impact of the different options for treatment on sexual functioning, both on the short — but also on the long term.

Chapter 2 outlines anatomy and current knowledge about the physiology of erection. Penile erection is a complex physiologic response depending upon the integration of vascular, neurologic and endocrine mechanisms. Although many aspects of the neurohumoral control of erection are still unknown, it is clear that erectile responses can be triggered by a variety of psychogenic and reflexogenic stimuli. They produce a neurally mediated vasodilatation of the penile blood vessels leading to an increase in blood flow, distension of sinusoidal spaces in the corpora cavernosa and reduction of venous drainage by the specific anatomy of the different parts of the venous system.

In chapter 3 diagnostic procedures and modalities for the treatment of impotence are discussed. The first step in the successful management of erectile dysfunction is identification of the cause(s). In the past most causes were thought to be psychogenic. However, recent advances in the understanding of the hemodynamics and neurophysiology of erection, as well as advances in diagnostic techniques, have made it clear that this is not true. Although the percentage of patients with psychogenic or organic impotence varies with the population under study, the overall feeling is that organic causes are more prevalent than was assumed previously. In no way however should this minimize the importance of psychologic factors to erectile function. Organic causes of impotence are frequently aggravated by the psychologic overlay.

The evaluation of organic causes of erectile dysfunction is reaching a high level of sophistication. The patient's history remains however the most important aspect of the evaluation. The history provides insight not only into the aetiology of the problem but also into the patient's acceptance of the various possible therapeutic options.

Visual sexual stimulation and nocturnal penile tumescence testing with modern devices may confirm the history obtained from the patient. By duplex scanning performed after intracavernous injection of papaverine (or another vasoactive drug) one may uncover in impairment in arterial blood flow. Venous leakage may be demonstrated by dynamic cavernosography.

Recent appreciation of the neuroanatomy and neurophysiology of erection makes it possible to assess neurogenic impotence. Of course clear cut neurologic deficits such as spinal cord injuries, multiple sclerosis, peroperative damage or traumatic injury are quite evident, but others require more extensive evaluation. Penile biothesiometry, dorsal nerve somatosensory evoked potential tests as well as demonstration of the bulbocavernosus reflex response are all clinically available methods of assessing neurogenic erectile dysfunction. For autonomic function there are as yet no conclusive tests.

Figure 4 in this chapter shows the diagnostic approach currently advocated by the Dutch Society for Impotence Research. In the near future this scheme will undoubtedly continue to be adapted. At present there is certainly no world-wide consensus in this regard.

The therapeutic arsenal for the treatment of erectile dysfunction has been markedly changed. One of the new therapies has been intracavernous injection of either papaverine alone or papaverine and phentolamine. Other agents (such as prostaglandin E1) are also being studied for this purpose.

The availability of erection prostheses was probably the single most important impetus to the development of "Erectile Dysfunction" as a subspeciality in urology. These prostheses continue to be modified and most of the newer devices attempt to preserve surgical simplicity while increasing the esthestic properties.

Vascular surgery for the treatment of erectile dysfunction has involved either microsurgical arterial bypass surgery or correction of the venous drainage of the penis. Bypass surgery usually implied the inferior epigastric artery as a neoarterial source, an anastomosis between this vessel and the interconnected dorsal artery and dorsal vein of the penis has gained popularity in the last few years. An other option is deep dorsal vein arterialization. Venous surgery is indicated in patients who describe life-long soft erections and show abnormal venous drainage on dynamic cavernosography.

Chapter 4 describes mythologic, religious, and cultural aspects of impotence before the present era. In the past, many forms of impotence have been attributed to supernatural factors. Although in modern society supernatural impotence seems to be only a marginal agent, it has been found that this cause of impotence still retains an important place in some groups of patients. Therefore it seems worthwhile when one approaches a patient with erectile dysfunction to examine his cultural background and how he conceptualizes and understands his erectile dysfunction. Such an approach may be of great help in the therapeutic process.

In chapter 5, comparison of simple Doppler blood pressure studies on the flaccid penis with the results of intracavernous injection of papaverine showed no correlation between these two variables. This confirms the limited value of blood pressure measurements on the non-erect penis. Intracavernous injection of papaverine in

combination with dynamic duplex-scanning of the penile vessels and corpora cavernosa provides a more significant test of the ability of the penile vasculature to produce an erection in the absence of venous pathology.

Chapter 6 assessed psychological, sexological, marital and medical aspects of intracavernous self-injection in the treatment of erectile impotence. Initially seventy-six percent of the patients (N=99) achieved a functional erection after injection. In the dosage determination- and training phase a quarter of the responders refused further treatment on grounds of inability to accept this form of treatment or because of varying responses, including recurrence of spontaneous erections. Some patients discontinued because of side effects such as ecchymoses and/or prolonged erection.

Self-injection treatment was associated with unchanged libido (59%), low injection frequency (59% once a month, 38% once a week and 3% twice a week), adequate erection rigidity (88%), and improvement (40%) or unchanged (55%) satisfaction with orgasm.

The reasons for discontinuation during the treatment phase were loss of sexual interest, partner resistance, loss of adequate responses or persistent problems with regard to self-injection, technically as well as psychologically. Side effects of self-injections included ecchymoses, nodule development and pain. Erection lasting longer than 6 hours occurred 11 times. Persistent fibrosis only occurred in 2 of these patients. Our long-term study demonstrated that one third of the responders do remarkably well. Couples who could not carry on sexual intercourse for several years are now able to do so on a regular basis. The self-injection therapy had also a positive impact upon their marital and psychological well-being.

Chapter 7 discusses the results of intracavernous self-injection of papaverine in the treatment of erectile impotence after major pelvic surgery. Erectile impotence is a well-known complication of major pelvic surgery. The incidence has been reported as 5 to 20% after excision of the rectum for benign disease, 33 to 100% after abdominoperineal rectum amputation, and 85% after radical cystectomy. In most patients this impotence after major pelvic surgery is due to nerve damage and an adequate reaction on intracavernous papaverine injection will follow. Erectile impotence is an important factor, but some other factors may also interfere with sexual function after major pelvic surgery. The emotional impact of a stoma may have a deleterious effect upon the libido. Practical problems, such as accidental leaking of urine or faeces, too much friction during intercourse, and the necessity to empty the stoma pouch before sexual activity may inhibit sexual function and need to be discussed with the surgeon, urologist or the enterostomal therapy nurse.

Chapter 8 details erectile dysfunction in patients with Peyronie's disease and congenital penile curvature. A bent penis may be accompanied by pain during erection and intromission problems leading to impotence and also pain felt by the partner. The cause is usually congenital or Peyronie's disease. Multiple and different therapeutic modalities have been advocated with various results. There is no agreement

about therapy nor about the first choice. We studied treatment comparing it with natural history. Fourty-four patients with a penile curvature were analyzed. The subjective symptoms were scored using a check list, objective symptoms were photographically documented. Patients were seen at 3 months intervals until a steady state was reached. When pain persisted longer than a year a Nesbitt operation followed.

It appeared that patients spontaneously showed a decline of their symptoms after 6–12 months. Twenty-three patients were just followed and 21 had an operation. All surgically treated patients were satisfied with regard to the functional and cosmetic aspects, however a complete straight penis was not accomplished in four patients. Since fifty percent of the patients showed a decline of symptoms we advocate no immediate treatment. When pain and/or dysfunction persist the Nesbitt operation is a safe and successful treatment.

Chapter 9 discusses the results of intracavernous injection of adrenaline in the management of priapism.

Until recently priapism was treated by making a shunt between corpus cavernosum and corpus spongiosum, or between corpus cavernosum and long saphenous vein. Such a procedure requires general or spinal anaesthesia. Also venous leak impotence may be one of the sequelae. For this reason we treated priapism by local adrenaline injection in analogy with intracavernous papaverine injection used in the treatment of erectile impotence. The short term efficacy of the adrenaline injection was apparent in six out of eight cases. In our opinion initial treatment of priapism by intracavernous injection of a sympathicomimetic drug is preferable to primary establishment of a shunt. In those with severe acidosis and ischaemia of the cavernous blood a shunt procedure may still be necessary.

The diagnosis and treatment of erectile dysfunction require a multidisciplinary approach, since the aetiology may be multifactorial. In erectile impotence pure organic causes are frequently aggravated by the psychological overlay. In a lot of patients detailed urological assessment therefore has to be supplemented with an evaluation conducted by a psychologist with expertise and interest in the field of sexual dysfunction. If at all possible, the sexual partner should be included: her story does not always coincide and early involvement of the partner facilitates therapeutic decisions to be made at a later date. Furthermore, the expectations and the outcome of urological interference with erectile dysfunction will be influenced by the preexistent quality of the sexual relationship. Future study towards this aspect may lead to a better selection for diagnostic procedures and therapy.

The diagnosis of erectile dysfunction requires not only a multi-disciplinary, but also a comprehensive approach. The members of the multidisciplinary team must put all the information together and after careful assessment of the data (not infrequently contradictory) make a judgement. However, despite the rapid increase in the understanding of erectile mechanisms and sophistication of tests, the final diagnosis upon which therapeutic decisions are based, has occassionally more of an art than a science.

Whether the treatment is hormonal replacement, a suction device, intracavernous self-injection, arterial reconstruction, venous ligation, prosthesis implantation, or psychosexual counseling, the patient and his partner will need time to adjust to the change restoration of erectile function will make in their lives. They need to know that failure of one treatment does not mean they need to give up. In fact, many patients initially will opt for a relatively non-invasive treatment and, if that does not work, try a different approach. A patient needs to know he has the urologist's support for his decision so that he will confidently return for advice if the first treatment becomes unsatisfactory.

Furthermore, the following practical recommandations can be given:

- plan enough time to get informed precisely about the patient's actual problem and its severity;
- try to involve the patient's partner as much as possible;
- provide clear and explicit information:
  speak in specific terms instead of being vague,
  use terms patients will understand;
- examine the own attitudes and feelings towards sexuality. If one feels uncomfortable in discussing erectile dysfunction and relational aspects of sexuality, refer the patient to a colleague;
- be aware of the fact that not all patients can nor wish to be helped.

Insight and information into the art to diagnose and treat patients with erectile dysfunction is the aim of this thesis. It is my hope that it will serve as a guideline for practitioners and a stimulus for future clinical research to improve the management of patients with erectile dysfunction.

CHAPTER 11

SAMENVATTING

In dit proefschrift wordt verslag gedaan van de resultaten van klinisch onderzoek met betrekking tot diagnose en behandeling van erectiestoornissen. In urologische zin omvat het begrip erectiestoornis:

- erectiele impotentie, het onvermogen een erectie te krijgen en/of te behouden in situaties waarin de man dit wil
- een kromme penis (in erectie) als gevolg van de ziekte van Peyronie of aangeboren afwijkingen
- priapisme, een te lang aanhoudende erectie die met pijn gepaard gaat en ook na orgasme niet verdwijnt.

De doelstellingen van het onderzoek worden beschreven in Hoofdstuk 1. Onze belangstelling ging in het bijzonder uit naar het effect van de verschillende behandelingswijzen van erectiele dysfunctie op het seksueel functioneren, zowel op korte als op lange termijn.

In hoofdstuk 2 wordt een overzicht gegeven van de anatomie van de penis en de huidige kennis op het gebied van de fysiologie van de erectie. De erectie van de penis is een complex fysiologisch gebeuren dat afhankelijk is van de integratie van vasculaire, neurogene en endocriene factoren. Veel aspecten van de neurohumorale sturingsmechanismen van de erectie zijn nog onopgehelderd. Wel is het duidelijk dat een erectie opgewekt kan worden door een veelheid van psychogene en reflexogene stimuli. Deze leiden via bepaalde zenuwbanen tot verwijding van de penisarterieën, toename van de bloedtoevoer, groter worden van de sinusoïdale ruimten in de corpora cavernosa en afname van de veneuze afvloed door specifieke kenmerken van het veneuze vaatstelsel van de penis.

In hoofdstuk 3 worden diagnostische methoden en behandelingswijzen van impotentie besproken. Voorwaarde voor het slagen van een behandeling van impotentie is zorgvuldig onderzoek naar de oorzaak. In het verleden dacht men dat deze meestal psychisch was. Toenemende kennis omtrent de hemodynamica en neurofysiologie van de erectie, geholpen door de ontwikkeling van steeds betere diagnostische technieken, heeft echter aangetoond dat dit niet zo is. Hoewel het percentage patiënten met psychogene of organische impotentie varieert per onderzoekspopulatie, is de gangbare mening dat een organische genese veel vaker voorkomt dan vroeger werd aangenomen. Het belang van psychologische factoren bij een patiënt met een erectiestoornis dient echter geenszins te worden onderschat. De symptomatologie van een organische erectiestoornis wordt vaak versterkt door psychische factoren. De diagnostische technieken richten zich op organische oorzaken en worden nog steeds verfijnd. Het belangrijkste onderdeel van de diagnostiek blijft echter een anamnese, die niet alleen inzicht biedt in de aetiologie, maar ook in de acceptatie van de verschillende therapeutische mogelijkheden. Visuele seksuele stimulatie en het meten van nachtelijke erecties kunnen de anamnese in objectieve zin bevestigen. Duplex scanning van de penisarteriën na intracaverneuze injectie met papaverine (of een andere vaso-actieve stof) kan een onvoldoende arteriële

instroom aan het licht brengen. Impotentie door veneuze lekkage kan aangetoond worden met behulp van dynamische cavernosografie.

Duidelijke neurologische aandoeningen zoals dwarslaesie, multiple sclerose of peroperatief ontstane zenuwlaesies behoeven in relatie met impotentieklachten meestal geen nader onderzoek. Om zuiver neurogene impotentie vast te stellen zijn het meten van de vibratie perceptie van de penis, "somatosensory evoked potential tests" van de nervus dorsalis penis en/of het vastleggen van de bulbocavernosus reflex geschikte methoden.

Figuur 4 in hoofdstuk 3 toont de diagnostische beslisboom zoals die voorgestaan wordt door de Nederlandse Vereniging voor Impotentie Onderzoek. In de nabije toekomst zal dit schema ongetwijfeld aanpassing behoeven. Anno 1991 is er zeker nog geen sprake van een algehele overeenstemming met betrekking tot een dergelijke diagnostische beslisboom.

Het arsenaal aan behandelingswijzen van erectiestoornissen is de laatste jaren aanzienlijk uitgebreid. Eén van de nieuwe behandelingen is die waarbij patiënten zichzelf een intracaverneuze injectie geven met ofwel alleen papaverine of een combinatie van papaverine met phentolamine. Andere medicamenten (zoals prostaglandine E1) worden in dit verband ook toegediend.

De ontwikkeling van inwendige erectieprothesen is waarschijnlijk de belangrijkste impuls geweest voor de ontwikkeling van het onderdeel "Erectiele Dysfunctie" binnen de urologie. Dergelijke prothesen worden nog steeds verbeterd. Bij het merendeel van de nieuwere ontwerpen wordt gepoogd de chirurgische techniek eenvoudig te houden en tegelijkertijd de functionele eigenschappen te optimaliseren.

Bij de behandeling van vasculaire erectiestoornissen worden zowel arteriële bypass-chirurgie als correctie van de veneuze afvloed van de penis toegepast. Bij bypass-chirurgie maakt men onder andere gebruik van de arteria epigastrica inferior; anastomose van deze arterie met de onderling verbonden arteria dorsalis penis en vena dorsalis penis (chirurgische a-v-fistel) wordt de laatste jaren gepropageerd. Een andere optie is arterialisatie van de diepe dorsale vene. Veneuze chirurgie is geïndiceerd bij patiënten met een slechte rigiditeit van de erectie, bij wie door middel van dynamisch cavernosografisch onderzoek een abnormale veneuze afvloed is aangetoond.

Hoofdstuk 4 beschrijft mythologische, religieuze en culturele aspecten van impotentie voor het begin van de 18e eeuw. In het verleden werden vele vormen van impotentie toegeschreven aan bovennatuurlijke factoren. Hoewel in het huidige tijdsgewricht deze zogenaamde bovennatuurlijke impotentie slechts van marginaal belang schijnt, lijkt deze oorzaak bij bepaalde groepen patiënten toch een belangrijke rol te spelen. Daarom is het zinvol om bij het afnemen van de anamnese bij een patiënt met een erectiestoornis zijn culturele achtergrond en het antwoord op de vraag hoe hij zijn stoornis beleeft te betrekken.

In hoofdstuk 5 worden eenvoudige Doppler bloeddrukmetingen van de slappe penis vergeleken met de resultaten van intracaverneuze injecties met papaverine; tussen deze twee variabelen werd geen verband gevonden. Dit bevestigt de beperkte waarde van bloeddrukmetingen van de niet-stijve penis. Intracaverneuze injectie met papaverine, in combinatie met dynamische duplex-scanning van de corpora cavernosa en de arteriae cavernosae, biedt waarschijnlijk een beter inzicht in het al dan niet bestaan van afwijkingen in de corpora en de arteriae cavernosae, en indirect in de kwaliteit van de toevoerende vaten.

Hoofdstuk 6 beschouwt psychologische, seksuologische en medische aspecten van intracaverneuze zelf-injectie bij de behandeling van erectiele impotentie. Aanvankelijk verkreeg 76% van de patiënten (N=99) een functionele erectie door middel van intracaverneuze injecties. Een kwart van hen zag van verdere behandeling af in de periode van het leren zelf-injiciëren vanwege de techniek zelf of omdat de respons sterk varieerde, of vanwege de terugkeer van spontane erecties. Sommige patiënten staakten de behandeling nadat zij bijwerkingen hadden ondervonden zoals ecchymosen en/of langdurige erecties. Op langere termijn, dat wil zeggen bij de patiënten die na het aanleren de behandeling bleven toepassen, ging deze samen met een onveranderd libido (59%), en een relatief lage injectiefrequentie (59% eens per maand, 38% eens per week en 3% tweemaal per week. De rigiditeit van de erectie was bij 88% steeds adequaat en bij 12% waren er kleine verschillen in de respons. De meerderheid was tevreden over de kwaliteit van het orgasme. De redenen om na verloop van tijd op te houden met het zelf-injiciëren waren verminderde libido, toch enige tegenzin bij de partner, een variërende of ontoereikende respons of voortdurende problemen met betrekking tot het zelf-injiciëren, zowel van technische als van psychologische aard. Bijwerkingen van de injecties waren ecchymosen, erecties die langer dan 6 uur duurden (11× in totaal), noduli in of onder de tunica albuginea en pijn. Slechts bij 2 patiënten ontstonden irreversibele fibrotische veranderingen in de tunica albuginea. Onze lange-termijn studie toont aan dat één derde van de mannen die starten met zelf-injecties het tot volle tevredenheid continueren. Paren die al jaren niet meer in staat waren tot coïtus, blijken dit nu weer te kunnen doen. De genoemde therapie bleek ook hun echtelijk en psychologisch welbevinden ten goede te komen.

Hoofdstuk 7 bespreekt de resultaten van de zelf gedane intracaverneuze injecties met papaverine ter behandeling van erectiele impotentie na radicale chirurgie in het kleine bekken. De incidentie wordt gesteld op 0–20% na excisie van het rectum bij een goedaardige aandoening, op 33–100% na abdominoperineale rectumamputatie, en op 85% na radicale cystectomie. In de meeste gevallen is deze impotentie het gevolg van zenuwbeschadiging en zal er een adequate reactie volgen op intracaverneuze injectie met papaverine. De erectiele impotentie is weliswaar een belangrijke factor, maar er zijn vele andere factoren die het seksueel functioneren na radicale bekkenchirurgie kunnen verstoren. Een stoma bijvoorbeeld kan emotioneel ingrijpend zijn en een nadelig effect op de libido hebben. Praktische problemen, zoals onverwacht verlies van urine of faeces tijdens het vrijen, loslaten van

het stomazakje bij de coïtus en de noodzaak om het stomazakje tevoren te legen kunnen remmend werken op het seksueel functioneren. Deze potentiële problemen dienen door de behandelend chirurg, uroloog of de stoma-verpleegkundige met patiënt en zijn partner besproken te worden.

Hoofdstuk 8 biedt een gedetailleerde beschrijving van erectiestoornissen bij patiënten met de ziekte van Peyronie of een aangeboren verkromming van de penis. Een kromme penis kan samen gaan met pijn tijdens de erectie en problemen opleveren bij het inbrengen van de penis. Dit kan tevens leiden tot impotentie maar ook tot pijn bij de partner. Verschillende therapieën werden toegepast, echter met uiteenlopende resultaten. Er bestaat geen overeenstemming over de beste therapie. Wij hebben de chirurgische behandeling bestudeerd in vergelijking met het natuurlijk beloop. Er werden 44 patiënten met een penisverkromming onderzocht. Subjectieve symptomen werden aangetekend op een checklist, objectieve werden fotografisch vastgelegd. De patiënten werden om de drie maanden gezien tot een stabiele toestand werd bereikt. Als de pijn langer dan een jaar aanhield volgde een operatie volgens de techniek beschreven door Nesbitt.

Bij veel patiënten bleek na 6–12 maanden een spontane afname van hun symptomen te zijn opgetreden. Drieentwintig patiënten werden uitsluitend vervolgd en 21 werden uiteindelijk geopereerd. Alle chirurgisch behandelde patiënten waren tevreden over de functionele en kosmetische aspecten; bij 4 patiënten werd echter geen volledig rechte penis verkregen. Aangezien 50% van de patiënten een spontane afname van hun symptomen toonde staan wij geen "vroege" chirurgische behandeling voor. Als de pijn en/of de erectiele dysfunctie voortduurt is een Nesbitt operatie echter veilig en succesvol gebleken.

Hoofdstuk 9 bespreekt de resultaten van intracaverneuze injecties met adrenaline bij de behandeling van priapisme. Tot voor kort werd priapisme behandeld door het aanleggen van een shunt tussen het corpus cavernosum en het corpus spongiosum, of tussen het corpus cavernosum en de vena saphena magna. Deze operaties vereisen algehele of ruggemergsanaesthesie. Impotentie door veneuze lekkage is één van de belangrijkste complicaties na een dergelijke operatie. Om deze redenen behandelden wij priapisme met locale adrenaline-injecties, analoog aan de intracaverneuze papaverine-injecties toegepast bij de behandeling van impotentie. Bij 6 van de 8 patiënten bleek deze adrenaline-injectie op korte termijn effectief. Ons inziens is daarom de initiële behandeling van priapisme middels een intracaverneuze injectie met een sympathicomimeticum te verkiezen boven het primair aanleggen van een shunt.

Diagnose en behandeling van erectiestoornissen vereisen een multidisciplinaire aanpak. Organische oorzaken worden vaak versterkt door psychologische factoren. Bij veel patiënten dient een gedetailleerd urologisch onderzoek uitgebreid te worden met een evaluatie door een psycholoog met expertise en interesse op het terrein van seksuele functiestoornissen. Indien enigszins mogelijk dient de partner

van de patiënt daarbij te worden betrokken: haar anamnese verschilt nogal eens, en het vroegtijdig betrekken van de partner vergemakkelijkt het nemen van beslissingen ten aanzien van de in een later stadium toe te passen behandeling. De verwachtingen en het uiteindelijke resultaat van urologische bemoeienis met erectiele dysfunctie worden waarschijnlijk beïnvloed door de preëxistente kwaliteit van de sexuele relatie. Nader onderzoek gericht op dit aspect zou wellicht tot een betere selectie van de methoden voor diagnostiek en behandeling kunnen leiden.

De diagnostiek van erectiestoornissen vereist een multidisciplinaire benadering. De leden van een dergelijk multidisciplinair team dienen te beschikken over alle informatie en pas na een zorgvuldige afweging van de (niet zelden tegenstrijdige) gegevens tot een diagnose en een voorstel met betrekking tot de toe te passen behandeling te komen. Niettegenstaande de toegenomen kennis van de erectie en de verfijning van diagnostische methoden is de diagnostiek en behandeling van erectiele dysfunctie bij tijd en wijle echter meer een kunst dan kunde.

Of de behandeling nu bestaat uit hormonale substitutie, vacuum-geïnduceerde erecties, intracaverneuze zelf-injectie, arteriële reconstructie, veneuze lek chirurgie, implantatie van een prothese of psychoseksuele hulpverlening, de patiënt en zijn partner zullen tijd nodig hebben om zich aan te passen aan de veranderingen die het terugkomen van erecties teweeg kan brengen. Zij dienen te weten dat als een bepaalde behandeling niet tot het gewenste resultaat leidt zij de moed niet behoeven op te geven. Veel patiënten zullen in eerste instantie de voorkeur geven aan een niet-invasieve behandeling en als die niet helpt voor een andere aanpak kiezen. De patiënt moet ervan overtuigd zijn dat zijn beslissing wordt gesteund, zodat hij vol vertrouwen terugkomt voor advies als de initiële behandeling onbevredigend mocht blijken te zijn.

Verder kunnen de volgende praktische aanbevelingen worden gegeven:
- neem voldoende tijd om geïnformeerd te geraken over het werkelijk probleem van de patiënt en de ernst daarvan;
- probeer zo veel mogelijk de partner erbij te betrekken;
- verschaf duidelijke en uitvoerige informatie:
  wees niet te vaag,
  gebruik specifieke op de patiënt toegesneden termen;
- overweeg de eigen attitude en gevoelens met betrekking tot sexualiteit. Als men zich onbehaaglijk voelt bij het bespreken van erectiele dysfunctie inclusief de daarmee samenhangende relationele aspecten, verwijs dan naar een collega;
- besef dat niet alle patiënten kunnen of willen worden geholpen.

Het doel van dit proefschrift is het verschaffen van inzicht en informatie over de eerder genoemde kunst van het diagnostiseren en behandelen van patiënten met

erectiestoornissen. Ik hoop dat het van dienst kan zijn in de dagelijkse praktijk, en een aanzet tot verder klinisch onderzoek naar de behandeling van patiënten met erectiestoornissen mag zijn.

APPENDIX

QUESTIONNAIRE BELONGING TO CHAPTER 6

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UROLOGIE
Prof.Dr. H.J.A. Mensink

Zeer geachte heer,

U werd op de afdeling urologie van het AZG in het recente verleden behandeld voor sexuele moeilijkheden. Er werd gestart met een behandeling door papaverine injecties. Wij willen graag inzicht krijgen in de korte en de lange termijn ervaringen van hen die begonnen zijn met deze behandeling. In verband hiermee verzoek ik u vriendelijk deze vragenlijst in te vullen. De gegevens zullen uiteraard vertrouwelijk door mij worden behandeld en slechts onder code, zonder uw persoonsgegevens, ter beschikking komen voor het onderzoek.

Algemene instructies bij het invullen van de vragenlijst.

Lees het onderstaande goed door vóór U de vragenlijst invult. Hoe vult u de vragenlijst in?

- U kiest een rustig moment waarop u alleen bent en er ruim de tijd voor kunt nemen.
- U vult de vragenlijst (A) in, in de volgorde waarin de bladzijden nu liggen.
- Mocht u na het lezen van de vragen alsnog besluiten **niet** mee te willen doen, wilt u dan wel de niet-ingevulde vragenlijst aan ons terugsturen?
- U geeft zo eerlijk mogelijk antwoord op de vragen. Er zijn geen goede of foute antwoorden; het gaat ons alleen om uw eigen mening.
- Denk niet te lang na over iedere vraag maar geef uw eerste spontane reactie.
- Het kan voorkomen dat u bepaalde vragen niet kunt beantwoorden omdat ze voor u niet van toepassing zijn. U kunt dit kenbaar maken door op deze vragen met NVT te antwoorden.
- Sla geen vragen over en probeer de lijst zo volledig mogelijk in te vullen.
- Als u de vragenlijst hebt ingevuld, kunt u deze in de bijgesloten antwoordenveloppe aan ons terugsturen. Een postzegel is niet nodig.
- Er is een aparte "partner"-vragenlijst bijgevoegd. Het is de bedoeling dat uw echtgenote of partner deze zelf en afzonderlijk invult. Het is de bedoeling dat zij deze lijst (B) apart in de daarvoor bestemde enveloppe naar ons terugstuurt.

Bij voorbaat dank voor uw medewerking.

Prof.Dr. H.J.A. Mensink

Nr.

Alvorens uw ervaringen met de behandeling aan de orde te stellen, zouden wij graag wat achtergrondinformatie van u hebben. Dit blad wordt na aankomst van een codenummer voorzien en gescheiden van de overige antwoorden verwerkt. Op deze wijze kunnen wij u volledige anonimiteit en vertrouwelijkheid garanderen.

1. Naam: .....

2. Geboortedatum: .....

3. Burgerlijke staat:
   (aankruisen wat voor u van toepassing is)
   - o ongehuwd
   - o gehuwd/samenwonend
   - o gescheiden/weduwnaar

4. Waar valt uw opleiding het best mee te vergelijken:
   - o lagere school
   - o lager beroepsonderwijs
   - o MULO/MAVO
   - o middelbaar beroepsonderwijs
   - o HAVO/VWO (HBS/LYCEUM/GYMNASIUM)
   - o hoger beroepsonderwijs
   - o wetenschappelijk onderwijs

Vragenlijst voor de man (A) Nr.

1. De volgende vragen gaan over de periode kort vóór en kort na het starten van de papaverine-injectie-behandeling.

1.1 Hoe is het besluit tot stand gekomen om te beginnen met papaverine-injecties?
- o het besluit ging hoofdzakelijk van mij uit
- o het besluit ging hoofdzakelijk van mijn partner uit
- o we hebben het besluit in onderling overleg genomen
- o het besluit is op sterke aandrang van iemand anders genomen bv de dokter, een vriend.....

1.2 Bent u, achteraf beschouwd, destijds voldoende voorgelicht over de papaverine-injecties?
- o zeker voldoende
- o voldoende
- o onvoldoende
- o zeker onvoldoende

1.3 Hoe lang na het aanleren in het ziekenhuis, paste u voor het eerst thuis een injectie toe?
- o binnen een week
- o binnen een maand
- o tussen 1-3 maanden
- o het is thuis nooit tot inspuiten gekomen

1.4 Kunt u een inschatting maken van het totaal aantal keren dat u zich een injectie met papaverine hebt toegediend?
- o nooit
- o minder dan 10×
- o 10-25×
- o 26-100×
- o meer dan 100×

1.5 In hoeverre verwachtte u destijds dat deze behandeling uw probleem zou kunnen oplossen?
- o ik verwachtte een volledige oplossing
- o ik verwachtte een aanzienlijke verbetering
- o ik verwachtte enige verbetering
- o ik verwachtte eigenlijk geen of nauwelijks verbetering

1.6 In hoeverre viel de pijn tijdens het inspuiten u mee/tegen
- o de pijn viel heel erg mee
- o de pijn viel wel mee
- o de pijn viel eigenlijk wat tegen
- o de pijn viel heel erg tegen

1.7 Indien u inmiddels de papaverine-injecties niet meer toepast, wilt u dan na vraag 1.7 doorgaan met vraag 3. Als u thans nog steeds papaverine-injecties toepast, kunt u doorgaan naar vraag 2.1.

Destijds hebt u besloten de papaverine-injecties niet meer toe te passen. Indien een van de volgende beweringen op u van toepassing is, wilt u dan een 'ja' aankruisen, indien een reden niet voor u van toepassing is, dan gaarne een 'nee' aankruisen.(U kunt meer dan een reden aankruisen) Het kan zijn dat geen enkele reden op u van toepassing is; dan kruist u steeds 'nee' aan.

		ja	**nee**
1.7.1	het kunstmatige van de behandeling	o	o
1.7.2	de terugkeer van normale erecties	o	o
1.7.3	het onbetrouwbaar resultaat na injectie	o	o
1.7.4	verlies van zin in sex	o	o
1.7.5	het gehannes met ampullen, naald en spuit	o	o
1.7.6	weerzin of bezwaren bij partner	o	o
1.7.7	niet goed(meer) zelf op kunnen zuigen en spuiten	o	o
1.7.8	steeds weer op controle moeten komen	o	o
1.7.9	niet meer voldoende reageren op papaverine	o	o
1.7.10	verhardingen in de penis	o	o
1.7.11	onderhuidse bloeduitstortingen	o	o
1.7.12	zeer langdurige erecties	o	o
1.7.13	geen partner meer hebben	o	o

1.7.14 anders: .....
(zelf in te vullen)

1.7.15 welke reden was het belangrijkst ...
(het nummer van de vraag invullen)

2. Vervolg vragen voor diegenen die papaverine-injecties zijn blijven toepassen.

Als u inmiddels nog steeds papaverine-injecties toepast, welke klachten of hinder heeft u daar dan bij?

		ja	nee
2.1.1	het kunstmatige van de behandeling	o	o
2.1.2			
2.1.3	het onbetrouwbaar resultaat na injectie	o	o
2.1.4	verlies van zin in sex	o	o
2.1.5	het gehannes met ampullen, naald en spuit	o	o
2.1.6	weerzin of bezwaren bij partner	o	o
2.1.7	niet goed(meer) zelf op kunnen zuigen en spuiten	o	o
2.1.8	steeds weer op controle moeten komen	o	o
2.1.9	niet meer voldoende reageren op papaverine	o	o
2.1.10	verhardingen in de penis	o	o
2.1.11	onderhuidse bloeduitstortingen	o	o
2.1.12	zeer langdurige erecties	o	o
2.1.13	geen partner meer hebben	o	o
2.1.14	anders: ..... (zelf in te vullen)		
2.1.15	welke klacht is voor u het belangrijkst: (het nummer van de vraag invullen)		

2.2 Hebt u gevoelens van schaamte tegenover uw partner met betrekking tot het toepassen van papaverine-injecties?

- o nee
- o eigenlijk niet
- o eigenlijk wel
- o ja

2.3 Wanneer maakt u terwille van het sexuele contact uw penis stijf?

- o tevoren als mijn partner er niet bij is
- o tijdens het vrijen
- o tevoren in het bijzijn van mijn partner

2.4 Hoe vaak leidt de papaverine-injectie niet tot het gewenste resultaat?
- soms
- een enkele keer
- eigenlijk nooit
- nooit

2.5 Hoe is het met de kwaliteit van de erecties?
- de erectie is stijver dan vroeger
- de erectie is zoals die vroeger was
- de erectie is minder stijf dan vroeger
- de erectie is veel slapper dan vroeger

2.6 Is uw zelfvertrouwen veranderd sinds u papaverine- injecties toepast?
- ja, toegenomen
- is iets toegenomen
- is iets afgenomen
- nee, afgenomen

2.7 Is uw sexuele belangstelling toegenomen sinds u papaverine-injecties toepast?
- ja, toegenomen
- iets toegenomen
- iets afgenomen
- nee, afgenomen

2.8 Is er sindsdien ook meer sexueel contact met uw partner?
- ja
- iets toegenomen
- iets afgenomen
- nee, afgenomen

2.9 Gemiddeld heb ik met mijn partner gemeenschap
- minder dan één maal per maand
- één tot twee maal per maand
- éénmaal per week
- vaker dan éénmaal per week

2.10 Hoe beoordeelt u het **aantal** keren dat u gemeenschap hebt?
- volstrekt onvoldoende
- voldoende
- onvoldoende
- volstrekt onvoldoende

2.11 Merkt u dat bij het vrijen uw gevoel van opwinding toegenomen is?

- ja, sterker geworden
- iets sterker geworden
- iets minder geworden
- nee, afgenomen

2.12 Is er iets veranderd met de ejaculatie (het klaarkomen)?

- beter
- beetje beter
- slechter
- veel slechter

2.13 Vindt u dat de sexuele relatie met uw partner veranderd is sinds u papaverine-injecties toepast?

- veel beter
- beter
- slechter
- veel slechter

2.14 Vindt u dat de relatie met uw partner sindsdien **over het algemeen** veranderd is?

- ja, verbeterd
- beetje beter
- slechter
- veel slechter

2.15 Kunt u thans zonder enig probleem de papaverine-injecties toedienen?

- ja
- nee, ik blijf moeilijkheden houden bij het spuiten en/of de voorbereidingen daartoe

2.16 Zoudt u, achteraf bekeken, opnieuw beginnen met het aanleren van zelfinjectie?

- ja, zeker
- ja, waarschijnlijk
- waarschijnlijk niet
- nee

2.17 Zou u de injecties anderen met hetzelfde probleem aanraden?

- ja, zeer zeker
- waarschijnlijk
- waarschijnlijk niet
- nee

3. Omschrijving van de toenmalige klacht.

Toelichting: impotentie betekent òfwel een **volledig** òfwel een **gedeeltelijk** onvermogen tot het krijgen en handhaven van een verstijving van de penis (erectie) tot aan de zaadlozing.

3.1 Was er bij u sprake van een **volledig potentieverlies** (= volledige afwezigheid van normale erectie)?
- o ja, altijd
- o meestal
- o een enkele keer
- o nooit

3.2 Was er bij u sprake van een **normale erectie** (=verstijving) **maar van een voortijdige verslapping van de penis?**
- o ja
- o soms
- o niet altijd
- o nee

3.3 Was er bij u sprake van **onvoldoende verstijving?**
- o ja, altijd
- o soms
- o een enkele keer
- o nooit

4. Wisselingen in de toenmalige klacht

Had u gemerkt dat één of meer van de volgende omstandigheden uw klacht in ongunstige zin beinvloeden? Indien dit op u van toepassing was, dan kunt u ook meer dan één der genoemde omstandigheden aankruisen.

		ja	**nee**
4.1	Uw lichamelijke toestand (bv. vermoeidheid)	o	o
4.2	Uw geestelijke toestand (bv. piekeren)	o	o
4.3	Het gebruik van medicijnen	o	o
4.4	Het gebruik van alcohol	o	o
4.5	Het gedrag van uw partner	o	o

Indien van toepassing:

4.6	Trad er in de periode van uw sexuele klachten wel een normale verstijving op bij zelfbevrediging?	o	o

5. Het verloop van de klachten indertijd

5.1 Wanneer zijn uw klachten begonnen? (maand, jaar) .....

5.2 **Hoe** zijn uw klachten indertijd begonnen?
- o geleidelijk in ernst toenemende klachten
- o af en toe optredende klachten
- o vrij plotselinge, blijvende klachten
- o plotseling, blijvende klachten

5.3 **Van wie** ging het initiatief uit om deskundige hulp te vragen?
- o van mijzelf
- o van mijn partner
- o van ons beiden

6. De verdere ontwikkeling van de klacht (vóór de papaverine-injecties)
Gelieve datgene aan te kruisen wat op u van toepassing is. U kunt ook meerdere mogelijkheden aankruisen.

6.1 Ik zelf vond het probleem met mijn potentie
- o lastig
- o nogal lastig
- o weinig lastig
- o niet lastig

6.2 Sinds mijn potentie minder was geworden
- o ben ik sexueel contact meer gaan vermijden
- o ben ik me juist extra gaan inspannen om het sexueel contact te laten slagen
- o geen van beiden

6.3 Sinds ik deze sexuele moeilijkheden had, voelde ik mij voor het sexuele contact meer onzeker dan vroeger
- o ja
- o eigenlijk wel
- o eigenlijk niet
- o nee

6.4 Sinds ik deze sexuele moeilijkheden had, lette ik er bij de seks veel meer op of mijn penis goed stijf zou worden
- o ja, zeer sterk
- o ja, enigzins

- eigenlijk niet
- helemaal niet

6.5 Sinds ik deze sexuele moeilijkheden had, werd mijn sexuele belangstelling (bv naar andere vrouwen kijken, fantaseren) over het algemeen
- sterker
- wat sterker
- wat minder
- minder

6.6 Toen ik deze potentieproblemen had, werd mijn belangstelling voor sexueel contact met mijn partner
- veel sterker
- iets sterker
- iets minder
- minder

6.7 Sinds ik deze sexuele moeilijkheden had, probeerde ik me voor of tijdens de seks extra op te peppen door middel van prikkelende verhalen, afbeeldingen of andere hulpmiddelen
- altijd
- meestal
- een enkele keer
- nooit

6.8 De houding van mijn partner ten opzichte van mijn potentieprobleem kan als volgt worden omschreven:
- zij had er begrip voor en gaf veel steun
- zij deed haar best er begrip voor te hebben, maar ze had het er toch moeilijk mee
- zij was wat afwijzend en onbegrijpend
- zij was sterk afwijzend en vol onbegrip

6.9 Degene die mijn problemen het ergste vond
- was ik zelf
- was mijn partner
- waren wij beiden

Nr.

Vragenlijst voor de partner (B)

Afzonderlijk door uw partner in te vullen en te verzenden in de bijgevoegde aparte enveloppe.

(Gelieve aan te kruisen wat voor u van toepassing is.)

1
- o mijn partner wilde papaverine injecties, van mij hoefde het niet zo nodig
- o het besluit tot injecties is door ons beiden genomen en we stonden er alletwee achter
- o ik had het graag, van mijn partner hoefde het niet zo

2
- o mijn partner schaamt zich eigenlijk nog steeds voor het feit dat hij papaverine-injecties toe moet passen
- o mijn partner schaamt zich er niet voor, hij vindt het eigenlijk iets vanzelfsprekends

3 Gemiddeld hebben wij gemeenschap:
- o minder dan éénmaal per maand
- o één tot twee maal per maand
- o ongeveer éénmaal per week
- o vaker dan éénmaal per week

4
- o ik ben best tevreden met het aantal keren dat we nu gemeenschap hebben
- o van mij hoeft het niet zo vaak
- o ik zou best wat vaker willen met mijn partner

5
- o mijn partner heeft, sinds hij papaverine-injecties toepast, veel meer belangstelling voor sex
- o ik merk niet dat mijn partner meer seksuele belangstelling heeft sinds hij injecties toepast

6
- o het seksuele contact met mijn partner gaat, dank zij de injecties, even gemakkelijk als tevoren
- o de samenleving is met de injecties moeilijker geworden dan toen het nog normaal ging

7 Sinds mijn partner papaverine-injecties toepast, is mijn beleving van het sexuele contact:
- o verbeterd
- o hetzelfde gebleven
- o verslechterd

8 o onze onderlinge verstandhouding is verbeterd sinds mijn partner papaverine-injecties toepast
o onze verstandhouding is hetzelfde gebleven
o onze verstandhouding is verslechterd

9 o ik vind die injecties een hele uitkomst
o het is mij toch wel tegengevallen

10 o als ik er opnieuw voorstond, zou ik mijn partner aanraden papaverine-injecties toe te passen
o als ik er opnieuw voorstond, zou ik mijn partner afraden papaverine-injecties toe te passen

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